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Title Page

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Volume 2 of 2

Revised Draft Report for Task Order No. UIC-7E

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

Sponsor: US Army Medical Materiel
Development Activity

Test Article: WR242511 Tartrate

Contract No.: DAMD17-92-C-2001

Study Director

Barry S. Levine, D.Sc., D.A.B.T.

In-Life Phase Completed On

January 14, 1994

Performing Laboratory

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19. ABSTRACT (Continue on reverse if necessary and identify by block number) This study evaluated the toxicity of WR242511 Tartrate in rats following thirteen weeks of daily oral (gavage) administration. Dose levels studied were 0 (vehicle control), 0.5, 1.5 and 4.5 mg base/kg/day. The primary treatment-related toxic effects of WR242511 were seen in the liver, lungs and RBCs. Males appeared more sensitive than females to the hepatotoxic effects of WR242511 administration. Microscopic liver lesions (hepatocyte degeneration and necrosis), and elevations in serum ALT and/or SDH levels were observed in mid and high dose males. Increased triglyceride and cholesterol levels in high dose females, and increased cholesterol levels in high dose males also suggested potential hepatocellular toxicity. Increases in total bile acids and alkaline phosphatase levels suggested hepatobiliary changes in high dose animals. Pulmonary microscopic lesions (alveolar histiocytosis) were observed in all WR242511-treated groups. These dose-related effects (hepatocyte degeneration and necrosis, and alveolar histiocytosis) probably contributed to the early deaths of seven out of ten high dose males. Treatment-related mild anemia was observed in mid dose and high dose animals. The lesser methemoglobinemic response seen in high dose males than in high dose females may have been secondary to the greater hepatotoxic effect in males, resulting in a reduction in the production of a direct methemoglobin-forming metabolite. Hemosiderosis in the spleen of high dose females was probably secondary to mild hemolytic anemia. Significant methemoglobin production was also observed in mid and high dose animals. Thymic lymphocyte depletion in high dose males was apparently secondary to stress produced by test article administration, but possibly could also be a direct treatment-related effect. Mild leukocytosis possibly secondary to stress and consisting of increased number of lymphocytes, neutrophils, monocytes, and/or eosinophils was seen in high dose animals and mid dose males. Thrombocytopenia was observed in all WR242511-treated groups. Because alveolar histiocytosis, thrombocytopenia, and hematology changes were seen at the low dose level, a no-adverse effect level of WR242511 could not be determined.					
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APPENDIX 4

Individual Body Weights and Body Weight Gains

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THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 107

GROUP: 1-M
DOSE: 0 (mg/kg)

SEX: MALE

ANIMAL #	DAY -3	DAY 0	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 43	DAY 49	DAY 56	DAY 63	DAY 70
301	185	214	291	341	403	441	474	507	534	558	564	591
302	191	233	306	365	416	466	500	534	573	595	613	634
303	193	229	301	358	398	442	465	499	524	554	556	579
304	204	238	321	392	453	496	530	583	605	635	638	666
305	208	236	301	360	407	447	459	500	526	543	548	572
306	183	217	286	334	393	431	454	503	539	565	568	593
307	204	241	317	378	437	484	519	554	577	601	610	633
308	199	233	298	349	398	439	465	496	528	564	572	604
309	196	233	314	383	444	495	526	576	609	640	654	694
310	198	233	298	346	397	433	452	491	522	537	532	570
MEAN	196	231	303	361	415	457	484	524	554	579	586	614
S.D.	8.2	8.7	11.3	19.0	22.0	25.7	31.1	34.9	34.2	36.7	40.7	42.0
N	10	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 107

GROUP: 1-M

SEX: MALE

DOSE: 0 (mg/kg)

ANIMAL # DAY 77 DAY 84 DAY 90

301	600	620	630
302	641	653	668
303	581	600	607
304	685	728	729
305	589	596	604
306	615	634	628
307	640	650	654
308	622	642	648
309	730	748	739
310	574	590	597

MEAN	628	646	650
S.D.	49.0	53.5	49.6
N	10	10	10

--: Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 107

GROUP: 2-M
DOSE: 0.5 (mg/kg)

SEX: MALE

ANIMAL #	DAY -3	DAY 0	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 43	DAY 49	DAY 56	DAY 63	DAY 70
321	187	218	295	353	420	472	499	527	562	590	589	620
322	177	212	282	338	402	445	464	522	551	574	591	623
323	206	239	317	382	431	478	498	547	586	605	618	650
324	193	226	289	351	400	433	459	511	537	569	567	593
325	189	219	283	332	374	414	445	490	532	556	560	600
326	200	224	290	345	399	448	475	518	512	551	538	585
327	201	230	252	257	340	406	445	486	518	542	552	576
328	195	228	293	339	379	409	426	466	493	509	513	555
329	198	232	299	360	408	457	466	517	558	581	585	614
330	210	243	312	360	403	441	465	509	545	566	579	598
MEAN	196	227	291	342	396	440	464	509	539	564	569	601
S.D.	9.7	9.5	17.9	33.0	25.7	25.1	22.8	23.2	27.1	26.9	30.0	26.8
N	10	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 107

GROUP: 2-M

SEX: MALE

DOSE: 0.5 (mg/kg)

ANIMAL # DAY 77 DAY 84 DAY 90

321	630	652	653
322	619	674	682
323	674	687	692
324	612	636	642
325	625	638	642
326	602	636	628
327	599	620	628
328	565	588	a
329	639	657	665
330	620	645	640

MEAN	619	643	652
S.D.	28.4	27.6	22.8
N	10	10	9

--: Data Unavailable a: Accidental Death

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 107

GROUP: 3-M
DOSE: 1.5 (mg/kg)

SEX: MALE

ANIMAL #	DAY -3	DAY 0	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 43	DAY 49	DAY 56	DAY 63	DAY 70
341	205	232	300	344	386	429	447	486	510	527	537	567
342	198	226	279	323	359	392	404	435	451	475	473	499
343	204	233	303	350	354	277	389	449	478	497	515	525
344	192	227	295	354	410	448	465	511	529	553	566	577
345	190	222	291	345	388	427	452	480	508	533	545	575
346	188	214	287	349	409	448	472	529	552	574	572	590
347	176	199	261	309	348	381	403	432	458	478	478	508
348	199	230	294	357	397	414	434	464	497	534	545	580
349	214	248	316	366	401	448	484	505	535	555	565	591
350	193	219	292	342	391	420	437	470	483	490	500	522
MEAN	196	225	292	344	384	408	439	476	500	522	530	553
S.D.	10.6	13.0	14.6	16.6	22.7	51.6	31.7	32.5	33.1	34.7	36.3	35.7
N	10	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 107

GROUP: 3-M
DOSE: 1.5 (mg/kg)

SEX: MALE

ANIMAL # DAY 77 DAY 84 DAY 90

341	582	596	596
342	508	513	c
343	540	536	563
344	604	619	621
345	594	619	619
346	616	636	645
347	519	534	528
348	604	630	635
349	607	637	646
350	533	541	538

MEAN	571	586	599
S.D.	41.1	49.3	45.5
N	10	10	9

--: Data Unavailable

c: Animal Found Dead

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 107

GROUP: 4-M

SEX: MALE

DOSE: 4.5 (mg/kg)

ANIMAL #	DAY -3	DAY 0	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 43	DAY 49	DAY 56	DAY 63	DAY 70
361	200	230	306	362	413	294	d	d	d	d	d	d
362	177	204	256	307	275	230	294	362	349	272	344	398
363	204	230	301	365	316	c	c	c	c	c	c	c
364	212	240	309	367	406	440	435	472	391	323	382	481
365	202	229	297	350	396	421	429	472	505	519	524	547
366	191	215	286	353	292	c	c	c	c	c	c	c
367	198	226	282	341	376	325	336	421	463	342	266	d
368	187	219	270	230	169	d	d	d	d	d	d	d
369	192	218	273	314	d	d	d	d	d	d	d	d
370	197	223	286	341	316	234	d	d	d	d	d	d
MEAN	196	223	287	333	329	324	374	432	427	364	379	475
S.D.	9.8	10.0	17.0	41.5	79.0	90.2	69.7	52.3	70.1	107.5	108.1	74.7
N	10	10	10	10	9	6	4	4	4	4	4	3

--: Data Unavailable

c: Animal Found Dead

d: Sacrificed Moribund

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 107

GROUP: 4-M

SEX: MALE

DOSE: 4.5 (mg/kg)

ANIMAL # DAY 77 DAY 84 DAY 90

361	d	d	d
362	436	419	407
363	c	c	c
364	537	493	441
365	565	588	598
366	c	c	c
367	d	d	d
368	d	d	d
369	d	d	d
370	d	d	d

MEAN 513 500 482

S.D. 67.9 84.7 101.9

N 3 3 3

--: Data Unavailable c: Animal Found Dead d: Sacrificed Moribund

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 107

GROUP: 1-F
DOSE: 0 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY -3	DAY 0	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 43	DAY 49	DAY 56	DAY 63	DAY 70
311	179	196	226	256	276	290	289	302	325	321	319	335
312	170	192	231	258	285	295	308	325	336	330	344	358
313	175	191	228	246	282	298	300	316	342	344	343	357
314	167	182	207	232	250	258	267	289	296	290	296	308
315	169	186	211	224	244	256	258	282	293	297	303	302
316	176	188	220	234	263	278	284	303	306	320	314	326
317	185	197	228	236	268	286	293	308	315	326	330	327
318	173	188	216	243	262	275	273	294	300	304	305	316
319	163	180	211	239	255	271	272	291	314	317	316	332
320	182	193	217	246	260	272	274	296	302	296	311	324
MEAN	174	189	220	241	265	278	282	301	313	315	318	329
S.D.	6.9	5.6	8.4	10.6	13.4	14.4	15.7	13.0	16.8	17.3	16.3	18.4
N	10	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 107

GROUP: 1-F
DOSE: 0 (mg/kg)

SEX: FEMALE

ANIMAL # DAY 77 DAY 84 DAY 90

311	327	338	343
312	349	352	367
313	356	383	404
314	313	318	311
315	317	316	318
316	328	328	329
317	342	351	348
318	317	320	322
319	336	345	344
320	323	325	319

MEAN	331	338	341
S.D.	14.5	20.9	28.1
N	10	10	10

--: Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 107

GROUP: 2-F

SEX: FEMALE

DOSE: 0.5 (mg/kg)

ANIMAL #	DAY -3	DAY 0	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 43	DAY 49	DAY 56	DAY 63	DAY 70
331	185	205	253	288	315	346	354	383	413	422	421	435
332	164	174	201	224	232	250	261	263	255	270	291	279
333	176	191	215	249	274	294	299	327	349	347	356	380
334	169	182	209	240	260	280	287	309	330	342	335	350
335	182	195	229	258	281	295	301	316	340	337	341	353
336	177	193	228	262	290	312	319	332	342	367	368	374
337	181	198	226	258	269	273	274	292	299	300	311	325
338	171	186	219	248	266	279	283	298	319	320	324	329
339	158	172	196	212	226	237	245	260	264	263	274	278
340	173	199	226	237	273	288	291	304	313	328	316	335
MEAN	174	190	220	248	269	285	291	308	322	330	334	344
S.D.	8.4	10.9	16.3	21.2	25.9	30.5	30.4	35.5	45.1	46.4	41.7	47.0
N	10	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 107

GROUP: 2-F
DOSE: 0.5 (mg/kg)

SEX: FEMALE

ANIMAL # DAY 77 DAY 84 DAY 90

331	453	459	467
332	289	297	295
333	384	388	403
334	354	356	366
335	370	365	364
336	379	389	399
337	333	341	339
338	341	341	343
339	281	290	291
340	340	352	347

MEAN	352	358	361
S.D.	49.3	48.4	52.4
N	10	10	10

--: Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 107				GROUP: 3-F				SEX: FEMALE				
				DOSE: 1.5 (mg/kg)								
ANIMAL #	DAY -3	DAY 0	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 43	DAY 49	DAY 56	DAY 63	DAY 70
351	170	181	212	232	243	256	261	272	277	290	287	300
352	176	188	221	236	250	271	279	294	289	305	320	327
353	183	200	246	268	272	295	301	326	329	356	354	370
354	190	198	221	243	257	273	277	295	320	323	319	335
355	160	180	208	245	275	312	317	335	351	353	370	379
356	172	184	221	245	259	264	276	302	276	311	319	334
357	176	192	209	235	254	271	275	303	308	303	336	338
358	172	190	218	248	258	271	279	301	299	306	316	325
359	167	180	206	221	240	269	259	264	262	279	285	290
360	181	201	240	278	291	317	332	348	363	366	372	395
MEAN	175	189	220	245	260	280	286	304	307	319	328	339
S.D.	8.6	8.2	13.4	16.9	15.5	20.7	23.7	26.2	33.3	29.6	30.4	33.3
N	10	10	10	10	10	10	10	10	10	10	10	10

---: Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 107

GROUP: 3-F
DOSE: 1.5 (mg/kg)

SEX: FEMALE

ANIMAL # DAY 77 DAY 84 DAY 90

351	304	312	306
352	332	348	350
353	383	395	400
354	348	351	350
355	393	399	402
356	332	341	336
357	337	330	337
358	321	326	317
359	281	281	292
360	413	418	423

MEAN	344	350	351
S.D.	41.0	42.6	43.8
N	10	10	10

--: Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 107

GROUP: 4-F
DOSE: 4.5 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY -3	DAY 0	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 43	DAY 49	DAY 56	DAY 63	DAY 70
371	188	203	249	262	282	311	326	334	355	352	360	370
372	169	185	201	222	244	257	255	282	292	280	296	315
373	173	188	219	250	265	275	287	300	316	319	315	326
374	157	170	193	218	235	248	255	272	276	290	287	299
375	177	190	230	249	272	283	271	332	336	318	331	342
376	168	180	203	201	211	223	224	232	236	246	242	260
377	176	191	222	239	239	248	261	276	273	282	294	293
378	171	183	207	222	246	260	269	269	287	288	292	296
379	181	195	230	254	265	277	295	311	321	332	325	341
380	180	191	215	224	227	249	260	276	286	294	299	317

MEAN	174	188	217	234	249	263	270	288	298	300	304	316
S.D.	8.5	8.9	16.7	19.5	22.1	24.3	27.5	31.3	34.6	30.4	31.4	31.0
N	10	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 107

GROUP: 4-F

SEX: FEMALE

DOSE: 4.5 (mg/kg)

ANIMAL # DAY 77 DAY 84 DAY 90

371	374	363	378
372	318	318	328
373	330	340	333
374	303	313	318
375	359	355	357
376	251	252	255
377	293	298	302
378	302	307	308
379	344	351	343
380	314	316	322

MEAN	319	321	324
S.D.	35.3	32.9	33.3
N	10	10	10

--: Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)*

STUDY: 107

GROUP: 1-M
DOSE: 0 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7**	DAY 14	DAY 21	DAY 28	DAY 35	DAY 43	DAY 49	DAY 56	DAY 63	DAY 70	DAY 77
301	77	50	62	38	33	33	27	24	6	27	9
302	73	59	51	50	34	34	39	22	18	21	7
303	72	57	40	44	23	34	25	30	2	23	2
304	83	71	61	43	34	53	22	30	3	28	19
305	65	59	47	40	12	41	26	17	5	24	17
306	69	48	59	38	23	49	36	26	3	25	22
307	76	61	59	47	35	35	23	24	9	23	7
308	65	51	49	41	26	31	32	36	8	32	18
309	81	69	61	51	31	50	33	31	14	40	36
310	65	48	51	36	19	39	31	15	-5	38	4
MEAN	73	57	54	43	27	40	29	26	6	28	14
S.D.	6.6	8.2	7.5	5.2	7.7	8.0	5.7	6.5	6.5	6.5	10.4
N	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

* Successive periods

** Baseline is Day 0

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)*

STUDY: 107

GROUP: 1-M
DOSE: 0 (mg/kg)

SEX: MALE

ANIMAL #	DAY 84	DAY 90	TOTAL GAIN
301	20	10	416
302	12	15	435
303	19	7	378
304	43	1	491
305	7	8	368
306	19	-6	411
307	10	4	413
308	20	6	415
309	18	-9	506
310	16	7	364
MEAN	18	4	420
S.D.	9.8	7.2	47.7
N	10	10	10

--: Data Unavailable

*Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)*

STUDY: 107

GROUP: 2-M
DOSE: 0.5 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7	DAY 14	DAY 21	DAY 28	DAY 35	DAY 43	DAY 49	DAY 56	DAY 63	DAY 70	DAY 77
321	77	58	67	52	27	28	35	28	-1	31	10
322	70	56	64	43	19	58	29	23	17	32	-4
323	78	65	49	47	20	49	39	19	13	32	24
324	63	62	49	33	26	52	26	32	-2	26	19
325	64	49	42	40	31	45	42	24	4	40	25
326	66	55	54	49	27	43	-6	39	-13	47	17
327	22	5	83	66	39	41	32	24	10	24	23
328	65	46	40	30	17	40	27	16	4	42	10
329	67	61	48	49	9	51	41	23	4	29	25
330	69	48	43	38	24	44	36	21	13	19	22
MEAN	64	51	54	45	24	45	30	25	5	32	17
S.D.	15.7	17.2	13.6	10.4	8.2	8.2	13.9	6.6	8.9	8.6	9.3
N	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

*Successive periods

**Baseline is Day 0

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL WEIGHT GAIN (Grams) *

STUDY: 107

GROUP: 2-M
DOSE: 0.5 (mg/kg)

SEX: MALE

ANIMAL #	DAY 84	DAY 90	TOTAL GAIN
----------	--------	--------	---------------

321	22	1	435
322	55	8	470
323	13	5	453
324	24	6	416
325	13	4	423
326	34	-8	404
327	21	8	398
328	23	a	--
329	18	8	433
330	25	-5	397

MEAN	25	3	425
S.D.	12.2	5.9	25.0
N	10	9	9

--: Data Unavailable a: Accidental Death

* Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)*

STUDY: 107

GROUP: 3-M
DOSE: 1.5 (mg/kg)

SEX: MALE

ANIMAL #	DAY 7**	DAY 14	DAY 21	DAY 28	DAY 35	DAY 43	DAY 49	DAY 56	DAY 63	DAY 70	DAY 77
341	68	44	42	43	18	39	24	17	10	30	15
342	53	44	36	33	12	31	16	24	-2	26	9
343	70	47	4	-77	112	60	29	19	18	10	15
344	68	59	56	38	17	46	18	24	13	11	27
345	69	54	43	39	25	28	28	25	12	30	19
346	73	62	60	39	24	57	23	22	-2	18	26
347	62	48	39	33	22	29	26	20	0	30	11
348	64	63	40	17	20	30	33	37	11	35	24
349	68	50	35	47	36	21	30	20	10	26	16
350	73	50	49	29	17	33	13	7	10	22	11
MEAN	67	52	40	24	30	37	24	22	8	24	17
S.D.	5.9	7.1	15.2	36.5	29.4	13.0	6.5	7.5	6.9	8.4	6.5
N	10	10	10	10	10	10	10	10	10	10	10

---: Data Unavailable

* Successive periods

** Baseline is Day 0

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)*

STUDY: 107

GROUP: 3-M
DOSE: 1.5 (mg/kg)

SEX: MALE

ANIMAL #	DAY 84	DAY 90	TOTAL GAIN
341	14	0	364
342	5	c	--
343	-4	27	330
344	15	2	394
345	25	0	397
346	20	9	431
347	15	-6	329
348	26	5	405
349	30	9	398
350	8	-3	319

MEAN	15	5	374
S.D.	10.4	9.7	40.0
N	10	9	9

--: Data Unavailable c: Animal Found Dead

* Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)*

STUDY: 107

GROUP: 4-M

SEX: MALE

DOSE: 4.5 (mg/kg)

ANIMAL #	DAY 7**	DAY 14	DAY 21	DAY 28	DAY 35	DAY 43	DAY 49	DAY 56	DAY 63	DAY 70	DAY 77
361	76	56	51	-119	d	d	d	d	d	d	d
362	52	51	-32	-45	64	68	-13	-77	72	54	38
363	71	64	-49	c	c	c	c	c	c	c	c
364	69	58	39	34	-5	37	-81	-68	59	99	56
365	68	53	46	25	8	43	33	14	5	23	18
366	71	67	-61	c	c	c	c	c	c	c	c
367	56	59	35	-51	11	85	42	-121	-76	d	d
368	51	-40	-61	d	d	d	d	d	d	d	d
369	55	41	d	d	d	d	d	d	d	d	d
370	63	55	-25	-82	d	d	d	d	d	d	d
MEAN	63	46	-6	-40	20	58	-5	-63	15	59	37
S.D.	9.0	31.2	48.2	59.8	30.5	22.3	56.3	56.3	67.2	38.2	19.0
N	10	10	9	6	4	4	4	4	4	3	3

--: Data Unavailable

c: Animal Found Dead

d: Sacrificed Moribund

* Successive periods

** Baseline is Day 0

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL WEIGHT GAIN (Grams)*

STUDY: 107

GROUP: 4-M
DOSE: 4.5 (mg/kg)

SEX: MALE

ANIMAL #	DAY 84	DAY 90	TOTAL GAIN
----------	--------	--------	---------------

361	d	d	--
362	-17	-12	203
363	c	c	--
364	-44	-52	201
365	23	10	369
366	c	c	--
367	d	d	--
368	d	d	--
369	d	d	--
370	d	d	--

MEAN	-13	-18	258
S.D.	33.7	31.4	96.4
N	3	3	3

--: Data Unavailable

c: Animal Found Dead

d: Sacrificed Moribund

* Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)*

STUDY: 107

GROUP: 1-F
DOSE: 0 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7**	DAY 14	DAY 21	DAY 28	DAY 35	DAY 43	DAY 49	DAY 56	DAY 63	DAY 70	DAY 77
311	30	30	20	14	-1	13	23	-4	-2	16	-8
312	39	27	27	10	13	17	11	-6	14	14	-9
313	37	18	36	16	2	16	26	2	-1	14	-1
314	25	25	18	8	9	22	7	-6	6	12	5
315	25	13	20	12	2	24	11	4	6	-1	15
316	32	14	29	15	6	19	3	14	-6	12	2
317	31	8	32	18	7	15	7	11	4	-3	15
318	28	27	19	13	-2	21	6	4	1	11	1
319	31	28	16	16	1	19	23	3	-1	16	4
320	24	29	14	12	2	22	6	-6	15	13	-1
MEAN	30	22	23	13	4	19	12	2	4	10	2
S.D.	5.0	7.9	7.4	3.0	4.7	3.5	8.4	7.2	6.9	6.8	8.1
N	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

* Successive periods

** Baseline is Day 0

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)*

STUDY: 107

GROUP: 1-F

SEX: FEMALE

DOSE: 0 (mg/kg)

ANIMAL #	DAY 84	DAY 90	TOTAL GAIN
----------	--------	--------	---------------

311	11	5	147
312	3	15	175
313	27	21	213
314	5	-7	129
315	-1	2	132
316	0	1	141
317	9	-3	151
318	3	2	134
319	9	-1	164
320	2	-6	126

MEAN	7	3	151
S.D.	8.1	8.9	26.8
N	10	10	10

--: Data Unavailable

* Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)*

STUDY: 107

GROUP: 2-F

SEX: FEMALE

DOSE: 0.5 (mg/kg)

ANIMAL #	DAY 7**	DAY 14	DAY 21	DAY 28	DAY 35	DAY 43	DAY 49	DAY 56	DAY 63	DAY 70	DAY 77
331	48	35	27	31	8	29	30	9	-1	14	18
332	27	23	8	18	11	2	-8	15	21	-12	10
333	24	34	25	20	5	28	22	-2	9	24	4
334	27	31	20	20	7	22	21	12	-7	15	4
335	34	29	23	14	6	15	24	-3	4	12	17
336	35	34	28	22	7	13	10	25	1	6	5
337	28	32	11	4	1	18	7	1	11	14	8
338	33	29	18	13	4	15	21	1	4	5	12
339	24	16	14	11	8	15	4	-1	11	4	3
340	27	11	36	15	3	13	9	15	-12	19	5
MEAN	31	27	21	17	6	17	14	7	4	10	9
S.D.	7.2	8.2	8.6	7.3	2.9	7.9	11.5	9.4	9.6	10.0	5.5
N	10	10	10	10	10	10	10	10	10	10	10

---: Data Unavailable

* Successive periods

** Baseline is Day 0

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)*

STUDY: 107

GROUP: 2-F
DOSE: 0.5 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 84	DAY 90	TOTAL GAIN
----------	--------	--------	---------------

331	6	8	262
332	8	-2	121
333	4	15	212
334	2	10	184
335	-5	-1	169
336	10	10	206
337	8	-2	141
338	0	2	157
339	9	1	119
340	12	-5	148

MEAN	5	4	172
S.D.	5.2	6.7	44.9
N	10	10	10

--: Data Unavailable

* Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL WEIGHT GAIN (Grams) *

STUDY: 107

GROUP: 3-F
DOSE: 1.5 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7**	DAY 14	DAY 21	DAY 28	DAY 35	DAY 43	DAY 49	DAY 56	DAY 63	DAY 70	DAY 77
351	31	20	11	13	5	11	5	13	-3	13	4
352	33	15	14	21	8	15	-5	16	15	7	5
353	46	22	4	23	6	25	3	27	-2	16	13
354	23	22	14	16	4	18	25	3	-4	16	13
355	28	37	30	37	5	18	16	2	17	9	14
356	37	24	14	5	12	26	-26	35	8	15	-2
357	17	26	19	17	4	28	5	-5	33	2	-1
358	28	30	10	13	8	22	-2	7	10	9	-4
359	26	15	19	29	-10	5	-2	17	6	5	-9
360	39	38	13	26	15	16	15	3	6	23	18
MEAN	31	25	15	20	6	18	3	12	9	12	5
S.D.	8.4	8.0	6.9	9.2	6.6	7.1	14.0	12.3	11.2	6.3	9.1
N	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

* Successive periods

** Baseline is Day 0

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL WEIGHT GAIN (Grams) *

STUDY: 107

GROUP: 3-F
DOSE: 1.5 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 84	DAY 90	TOTAL GAIN
----------	--------	--------	---------------

351	8	-6	125
352	16	2	162
353	12	5	200
354	3	-1	152
355	6	3	222
356	9	-5	152
357	-7	7	145
358	5	-9	127
359	0	11	112
360	5	5	222

MEAN	6	1	162
S.D.	6.4	6.3	39.8
N	10	10	10

---: Data Unavailable

* Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)*

STUDY: 107

GROUP: 4-F
DOSE: 4.5 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 7**	DAY 14	DAY 21	DAY 28	DAY 35	DAY 43	DAY 49	DAY 56	DAY 63	DAY 70	DAY 77
371	46	13	20	29	15	8	21	-3	8	10	4
372	16	21	22	13	-2	27	10	-12	16	19	3
373	31	31	15	10	12	13	16	3	-4	11	4
374	23	25	17	13	7	17	4	14	-3	12	4
375	40	19	23	11	-12	61	4	-18	13	11	17
376	23	-2	10	12	1	8	4	10	-4	18	-9
377	31	17	0	9	13	15	-3	9	12	-1	0
378	24	15	24	14	9	0	18	1	4	4	6
379	35	24	11	12	18	16	10	11	-7	16	3
380	24	9	3	22	11	16	10	8	5	18	-3
MEAN	29	17	15	15	7	18	9	2	4	12	3
S.D.	9.1	9.3	8.4	6.2	9.1	16.7	7.4	10.5	8.2	6.5	6.6
N	10	10	10	10	10	10	10	10	10	10	10

---: Data Unavailable

* Successive periods

** Baseline is Day 0

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL WEIGHT GAIN (Grams)*

STUDY: 107

GROUP: 4-F
DOSE: 4.5 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 84	DAY 90	TOTAL GAIN
----------	--------	--------	---------------

371	-11	15	175
372	0	10	143
373	10	-7	145
374	10	5	148
375	-4	2	167
376	1	3	75
377	5	4	111
378	5	1	125
379	7	-8	148
380	2	6	131

MEAN	3	3	137
S.D.	6.5	6.9	28.6
N	10	10	10

--: Data Unavailable

* Successive periods

DRAFT

APPENDIX 5

Individual Food Consumption Data

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 1-M
DOSE: 0 (mg/kg)

SEX: MALE

ANIMAL #	DAY 0**	DAY 7	DAY 14	DAY 21	DAY 28	DAY 31	DAY 43	DAY 49	DAY 56	DAY 59	DAY 70	DAY 77
301	23	29	31	32	32	34	33	33	34	36	33	35
302	24	29	30	30	31	34	33	33	33	36	33	33
303	23	26	28	27	29	33	29	29	31	30	29	29
304	26	30	35	33	32	38	36	34	35	35	35	36
305	23	25	29	29	29	30	29	31	29	31	30	30
306	22	26	28	28	28	35	29	27	28	31	27	28
307	24	27	30	30	31	34	33	31	31	39	31	30
308	24	29	29	28	29	32	32	31	33	33	33	33
309	24	29	36	35	35	37	38	37	37	39	37	40
310	22	26	28	28	30	31	30	30	30	33	30	31
MEAN	24	28	30	30	31	34	32	32	32	34	32	33
S.D.	1.2	1.8	2.9	2.6	2.1	2.5	3.1	2.8	2.8	3.2	3.0	3.7
N	10	10	10	10	10	10	10	10	10	10	10	10

---: Data Unavailable

* Successive periods

** Food was weighed in on Day -6

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 1-M
DOSE: 0 (mg/kg)
ANIMAL # DAY 84 DAY 87

SEX: MALE

301	33	38
302	28	34
303	29	32
304	41	36
305	29	34
306	28	31
307	29	33
308	36	36
309	40	41
310	30	33

MEAN	32	35
S.D.	5.0	3.0
N	10	10

--: Data Unavailable

*Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 2-M

SEX: MALE

DOSE: 0.5(mg/kg)

ANIMAL #	DAY 0**	DAY 7	DAY 14	DAY 21	DAY 28	DAY 31	DAY 43	DAY 49	DAY 56	DAY 59	DAY 70	DAY 77
321	22	27	31	33	36	35	32	34	36	37	34	34
322	22	26	29	31	31	29	32	32	33	37	32	31
323	25	29	33	32	33	35	34	38	35	41	33	35
324	23	26	29	29	29	32	32	32	33	36	30	33
325	21	25	28	27	29	29	32	32	33	32	32	33
326	21	25	28	29	33	35	32	21	36	36	30	32
327	24	24	13	29	31	33	32	30	31	34	31	31
328	23	26	26	26	25	27	27	27	28	31	30	29
329	24	28	31	32	34	34	35	35	36	37	35	37
330	25	27	29	29	29	32	30	30	31	35	31	31
MEAN	23	26	28	30	31	32	32	31	33	36	32	33
S.D.	1.5	1.5	5.5	2.3	3.2	2.9	2.2	4.7	2.7	2.8	1.8	2.3
N	10	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

* Successive periods

** Food was weighed in on Day -6

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 2-M
DOSE: 0.5 (mg/kg)
ANIMAL # DAY 84 DAY 87

SEX: MALE

321	34	35
322	33	35
323	35	36
324	35	34
325	31	31
326	38	33
327	32	33
328	41	32
329	36	39
330	32	33

MEAN	35	34
S.D.	3.1	2.3
N	10	10

--: Data Unavailable

*Successive periods

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams) *

STUDY: 107

GROUP: 3-M
DOSE: 1.5 (mg/kg)

SEX: MALE

ANIMAL #	DAY 0**	DAY 7	DAY 14	DAY 21	DAY 28	DAY 31	DAY 43	DAY 49	DAY 56	DAY 59	DAY 70	DAY 77
341	26	29	28	28	29	30	31	30	30	32	30	30
342	23	24	25	24	24	26	25	25	29	29	27	26
343	24	27	29	28	6	33	35	30	31	35	29	30
344	23	27	30	29	30	30	31	29	30	34	31	32
345	23	27	27	28	29	30	29	29	31	32	32	33
346	23	26	28	30	30	34	33	32	32	35	29	31
347	21	24	24	24	25	26	26	25	25	28	26	26
348	23	26	28	29	27	33	30	31	32	37	35	34
349	25	28	29	28	29	32	32	32	32	37	31	32
350	22	28	31	33	29	30	29	26	27	31	28	29
MEAN	23	27	28	28	26	30	30	29	30	33	30	30
S.D.	1.4	1.6	2.1	2.6	7.3	2.8	3.0	2.7	2.3	3.1	2.6	2.7
N	10	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

* Successive periods

** Food was weighed in on Day -6

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams) *

STUDY: 107

GROUP: 3-M

SEX: MALE

DOSE: 1.5 (mg/kg)

ANIMAL # DAY 84 DAY 87

341	30	31
342	27	19
343	28	31
344	33	30
345	31	31
346	31	34
347	25	27
348	34	36
349	32	37
350	22	29

MEAN	29	31
S.D.	3.8	5.1
N	10	10

--: Data Unavailable

*Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams) *

STUDY: 107

GROUP: 4-M

SEX: MALE

DOSE: 4.5 (mg/kg)

ANIMAL #	DAY 0 **	DAY 7	DAY 14	DAY 21	DAY 28	DAY 31	DAY 43	DAY 49	DAY 56	DAY 59	DAY 70	DAY 77
361	25	28	30	31	7	d	d	d	d	d	d	d
362	21	23	25	15	6	20	29	18	4	17	30	26
363	25	27	31	16	c	c	c	c	c	c	c	c
364	23	27	30	29	30	32	31	11	8	17	37	37
365	24	25	27	27	26	29	29	27	28	30	31	30
366	21	25	28	15	c	c	c	c	c	c	c	c
367	24	25	28	28	17	11	34	31	9	1	d	d
368	22	23	14	9	d	d	d	d	d	d	d	d
369	20	23	24	d	d	d	d	d	d	d	d	d
370	22	24	26	19	4	d	d	d	d	d	d	d
MEAN	23	25	26	21	15	23	31	22	12	16	33	31
S.D.	1.8	1.8	4.9	7.9	11.1	9.5	2.4	9.0	10.7	11.9	3.8	5.6
N	10	10	10	9	6	4	4	4	4	4	3	3

--: Data Unavailable

c: Animal Found Dead

d: Sacrificed Moribund

* Successive periods

** Food was weighed in on Day -6

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams) *

STUDY: 107

GROUP: 4-M
DOSE: 4.5 (mg/kg)
ANIMAL # DAY 84 DAY 87

SEX: MALE

361	d	d
362	21	20
363	c	c
364	26	12
365	31	34
366	c	c
367	d	d
368	d	d
369	d	d
370	d	d

MEAN	26	22
S.D.	5.0	11.1
N	3	3

--: Data Unavailable

c: Animal Found Dead

d: Sacrificed Moribund

*Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

D E

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 1-F

SEX: FEMALE

DOSE: 0 (mg/kg)

ANIMAL #	DAY 0**	DAY 7	DAY 14	DAY 21	DAY 28	DAY 31	DAY 43	DAY 49	DAY 56	DAY 59	DAY 70	DAY 77
311	20	21	23	20	21	21	24	20	20	22	21	20
312	20	21	23	22	23	25	25	22	23	28	22	21
313	19	21	23	22	23	25	23	24	23	23	24	23
314	19	19	22	22	21	22	22	19	20	23	19	20
315	18	17	18	17	18	19	19	19	19	22	18	20
316	17	17	22	20	19	20	22	21	21	21	17	20
317	19	19	23	23	23	22	25	25	26	34	23	23
318	18	19	25	19	22	23	20	20	23	23	18	19
319	19	19	20	20	21	21	23	23	22	23	22	25
320	18	19	22	18	19	19	22	20	20	23	19	19
MEAN	19	19	22	20	21	22	23	21	22	24	20	21
S.D.	0.9	1.5	1.9	1.9	1.8	2.2	2.0	2.1	2.1	3.9	2.4	2.0
N	10	10	10	10	10	10	10	10	10	10	10	10

---: Data Unavailable

* Successive periods

** Food was weighed in on Day -6

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 1-F
DOSE: 0 (mg/kg)

SEX: FEMALE

ANIMAL # DAY 84 DAY 87

311	23	23
312	20	23
313	24	31
314	24	22
315	18	20
316	19	20
317	22	30
318	23	22
319	22	22
320	19	22

MEAN	21	24
S.D.	2.2	3.8
N	10	10

--: Data Unavailable

*Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams) *

STUDY: 107

GROUP: 2-F

SEX: FEMALE

DOSE: 0.5 (mg/kg)

ANIMAL #	DAY 0 **	DAY 7	DAY 14	DAY 21	DAY 28	DAY 31	DAY 43	DAY 49	DAY 56	DAY 59	DAY 70	DAY 77
331	21	25	26	25	28	27	27	26	27	28	23	26
332	19	19	21	19	20	21	19	17	20	24	19	19
333	19	19	23	22	23	26	24	25	24	26	24	24
334	21	20	22	21	21	23	23	23	23	24	22	22
335	20	23	24	22	25	31	25	28	26	28	24	25
336	20	21	25	23	28	25	23	24	26	28	21	24
337	20	23	23	21	23	26	21	23	26	29	20	22
338	20	21	21	21	21	25	21	24	23	26	20	21
339	17	18	19	17	18	26	21	18	20	21	19	19
340	21	19	20	22	21	21	22	20	24	24	20	22
MEAN	20	21	22	21	23	25	23	23	24	26	21	22
S.D.	1.2	2.3	2.2	2.2	3.3	3.0	2.3	3.5	2.5	2.5	1.9	2.4
N	10	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

* Successive periods

** Food was weighed in on Day -6

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 2-F

SEX: FEMALE

DOSE: 0.5 (mg/kg)

ANIMAL # DAY 84 DAY 87

331	26	29
332	20	19
333	23	26
334	21	25
335	24	27
336	24	25
337	21	23
338	23	21
339	18	20
340	24	23

MEAN	22	24
S.D.	2.4	3.2
N	10	10

--: Data Unavailable

*Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 3-F
DOSE: 1.5 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 0**	DAY 7	DAY 14	DAY 21	DAY 28	DAY 31	DAY 43	DAY 49	DAY 56	DAY 59	DAY 70	DAY 77
351	17	19	20	19	20	22	18	18	19	24	18	18
352	18	18	20	18	19	24	19	16	20	24	21	21
353	20	23	23	21	22	28	24	21	24	26	21	23
354	20	20	22	21	20	24	23	24	24	26	23	24
355	18	17	21	23	25	23	22	23	23	26	24	23
356	20	21	22	20	21	23	25	19	22	27	21	22
357	20	20	21	22	22	29	22	19	21	31	23	18
358	19	18	22	22	21	21	23	21	24	38	23	24
359	19	22	23	22	23	21	21	17	22	21	22	21
360	22	22	23	24	24	28	26	24	25	25	26	30
MEAN	19	20	22	21	22	24	22	20	22	27	22	22
S.D.	1.4	2.0	1.2	1.8	1.9	3.0	2.5	2.9	2.0	4.7	2.2	3.4
N	10	10	10	10	10	10	10	10	10	10	10	10

---: Data Unavailable

* Successive periods

** Food was weighed in on Day -6

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams) *

STUDY: 107

GROUP: 3-F

SEX: FEMALE

DOSE: 1.5 (mg/kg)

ANIMAL # DAY 84 DAY 87

351	20	19
352	22	22
353	23	25
354	22	22
355	22	21
356	21	20
357	20	21
358	27	20
359	20	19
360	29	29

MEAN 23 22

S.D. 3.1 3.1

N 10 10

--: Data Unavailable

*Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams) *

STUDY: 107

GROUP: 4-F

SEX: FEMALE

DOSE: 4.5 (mg/kg)

ANIMAL #	DAY 0 **	DAY 7	DAY 14	DAY 21	DAY 28	DAY 31	DAY 43	DAY 49	DAY 56	DAY 59	DAY 70	DAY 77
371	21	22	22	20	23	24	23	22	21	22	23	22
372	20	21	19	20	20	35	23	21	22	33	24	26
373	18	18	20	17	19	23	19	18	20	22	19	20
374	18	19	17	17	17	20	20	17	22	23	18	19
375	22	22	21	20	20	23	24	20	19	25	20	25
376	18	18	15	16	16	24	18	15	18	17	17	18
377	19	21	18	17	17	19	18	17	17	22	18	21
378	19	19	19	18	20	21	18	22	19	21	19	21
379	18	21	21	16	19	26	23	25	22	24	22	23
380	18	20	18	15	18	23	21	19	22	19	23	21
MEAN	19	20	19	18	19	24	21	20	20	23	20	22
S.D.	1.4	1.5	2.1	1.8	2.0	4.4	2.4	3.0	1.9	4.3	2.5	2.5
N	10	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

* Successive periods

** Food was weighed in on Day -6

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL DAILY FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 4-F

SEX: FEMALE

DOSE: 4.5 (mg/kg)

ANIMAL # DAY 84 DAY 87

371	22	21
372	24	24
373	20	17
374	21	20
375	26	24
376	16	15
377	21	18
378	21	19
379	31	21
380	24	21

MEAN 23 20

S.D. 4.0 2.9

N 10 10

--: Data Unavailable

*Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 1-M

SEX: MALE

DOSE: 0 (mg/kg)

ANIMAL #	DAY 0**	DAY 7	DAY 14	DAY 21	DAY 28	DAY 31	DAY 43	DAY 49	DAY 56	DAY 59	DAY 70	DAY 77
301	139	200	219	221	226	102	263	197	240	107	263	246
302	142	201	210	212	217	103	263	195	234	109	267	228
303	136	185	195	192	200	99	235	173	214	91	234	206
304	153	211	246	230	226	113	286	204	244	105	279	254
305	136	176	205	200	201	90	234	187	204	94	241	211
306	131	183	193	199	199	106	232	160	194	92	217	194
307	143	187	207	210	219	102	263	185	215	118	245	207
308	141	200	206	197	204	95	259	184	234	100	261	231
309	146	201	250	243	248	110	300	223	260	117	292	279
310	130	185	193	195	208	93	236	179	209	99	239	220
MEAN	140	193	212	210	215	101	257	189	225	103	254	228
S.D.	6.9	11.1	20.5	16.8	15.6	7.3	23.3	17.4	20.7	9.7	22.6	25.9
N	10	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

* Successive periods

** Food was weighed in on Day -6

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 1-M

SEX: MALE

DOSE: 0 (mg/kg)

ANIMAL # DAY 84 DAY 87

301	234	115
302	197	102
303	202	97
304	286	108
305	203	103
306	196	92
307	204	99
308	251	108
309	277	124
310	207	99

MEAN 226 105

S.D. 34.3 9.4

N 10 10

--: Data Unavailable

*Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL FOOD CONSUMPTION (Grams) *

STUDY: 107

GROUP: 2-M

SEX: MALE

DOSE: 0.5 (mg/kg)

ANIMAL #	DAY 0 **	DAY 7	DAY 14	DAY 21	DAY 28	DAY 31	DAY 43	DAY 49	DAY 56	DAY 59	DAY 70	DAY 77
321	134	189	214	234	250	106	259	202	253	112	270	237
322	130	180	203	215	218	88	255	190	228	110	258	216
323	151	205	232	227	231	105	271	225	248	122	264	242
324	137	179	204	203	202	96	257	192	232	108	236	228
325	128	172	194	189	206	88	252	194	230	95	258	228
326	127	175	195	204	232	106	253	125	253	108	239	225
327	141	165	89	204	219	98	252	180	217	102	245	214
328	139	182	179	180	176	81	218	162	196	92	243	204
329	142	195	216	225	236	101	279	208	252	112	282	258
330	148	192	202	203	200	97	242	179	215	104	249	218
MEAN	138	183	193	208	217	97	254	186	232	107	254	227
S.D.	8.1	11.9	39.2	17.0	21.6	8.6	16.3	27.4	19.3	8.7	14.7	15.6
N	10	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

* Successive periods

** Food was weighed in on Day -6

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 2-M

SEX: MALE

DOSE: 0.5 (mg/kg)

ANIMAL # DAY 84 DAY 87

321	241	105
322	234	105
323	247	107
324	245	103
325	218	94
326	269	99
327	224	98
328	287	96
329	250	118
330	223	100

MEAN 244 103

S.D. 21.5 6.9

N 10 10

--: Data Unavailable

*Successive periods

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL FOOD CONSUMPTION (Grams) *

STUDY: 107

GROUP: 3-M

SEX: MALE

DOSE: 1.5 (mg/kg)

ANIMAL #	DAY 0 **	DAY 7	DAY 14	DAY 21	DAY 28	DAY 31	DAY 43	DAY 49	DAY 56	DAY 59	DAY 70	DAY 77
341	154	200	197	194	204	89	250	177	211	96	243	211
342	136	167	173	169	170	78	202	152	201	86	218	183
343	145	189	204	195	41	99	280	177	217	105	232	207
344	140	192	209	201	208	91	250	176	208	102	247	226
345	138	186	192	193	200	90	234	175	219	96	257	228
346	136	184	198	212	208	101	264	190	222	104	228	220
347	126	169	171	169	174	78	207	151	177	85	207	181
348	137	182	196	203	192	99	236	186	224	111	277	239
349	149	194	203	196	204	95	255	193	223	110	249	226
350	132	196	215	229	203	91	229	157	190	93	225	206
MEAN	139	186	196	196	180	91	241	173	209	99	238	213
S.D.	8.2	10.9	14.2	17.9	50.8	8.1	24.3	15.2	15.7	9.2	20.5	19.1
N	10	10	10	10	10	10	10	10	10	10	10	10

---: Data Unavailable

* Successive periods

** Food was weighed in on Day -6

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 3-M

SEX: MALE

DOSE: 1.5 (mg/kg)

ANIMAL # DAY 84 DAY 87

341	208	93
342	186	56
343	196	93
344	231	91
345	215	93
346	216	101
347	178	80
348	235	107
349	227	111
350	157	87

MEAN	205	91
S.D.	25.3	15.4
N	10	10

--: Data Unavailable

*Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 4-M

SEX: MALE

DOSE: 4.5 (mg/kg)

ANIMAL #	DAY 0**	DAY 7	DAY 14	DAY 21	DAY 28	DAY 31	DAY 43	DAY 49	DAY 56	DAY 59	DAY 70	DAY 77
361	149	194	212	218	51	d	d	d	d	d	d	d
362	128	159	172	106	44	60	231	105	29	50	240	181
363	148	192	215	109	c	c	c	c	c	c	c	c
364	140	191	208	200	210	97	244	66	56	51	293	257
365	143	176	190	189	184	88	231	161	198	89	247	213
366	128	172	196	102	c	c	c	c	c	c	c	c
367	146	177	195	195	117	34	271	183	63	4	d	d
368	132	164	99	60	d	d	d	d	d	d	d	d
369	120	162	166	d	d	d	d	d	d	d	d	d
370	134	166	184	132	28	d	d	d	d	d	d	d
MEAN	137	175	184	146	106	70	244	129	87	49	260	217
S.D.	9.9	13.1	33.9	55.7	77.4	28.6	18.9	53.2	75.8	34.8	28.8	38.2
N	10	10	10	9	6	4	4	4	4	4	3	3

--: Data Unavailable

c: Animal Found Dead

d: Sacrificed Moribund

* Successive periods

** Food was weighed in on Day -6

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 4-M

SEX: MALE

DOSE: 4.5 (mg/kg)

ANIMAL # DAY 84 DAY 87

361	d	d
362	145	61
363	c	c
364	182	35
365	215	102
366	c	c
367	d	d
368	d	d
369	d	d
370	d	d

MEAN	181	66
S.D.	35.0	33.8
N	3	3

--: Data Unavailable

c: Animal Found Dead

d: Sacrificed Moribund

*Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 1-F
DOSE: 0 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 0**	DAY 7	DAY 14	DAY 21	DAY 28	DAY 31	DAY 43	DAY 49	DAY 56	DAY 59	DAY 70	DAY 77
311	120	146	160	140	144	64	189	121	140	66	168	138
312	117	148	163	152	161	74	200	129	158	83	173	148
313	113	144	158	152	164	75	182	141	161	69	190	158
314	111	134	156	151	144	66	178	115	141	68	155	143
315	108	118	123	119	123	58	153	114	133	65	141	138
316	103	120	154	137	133	59	178	124	145	63	136	141
317	112	131	159	162	163	67	200	151	179	101	181	160
318	110	134	172	130	153	70	160	120	158	70	147	133
319	111	135	137	137	147	62	184	140	151	69	176	172
320	106	136	155	125	134	58	177	121	137	69	150	133
MEAN	111	135	154	141	147	65	180	128	150	72	162	146
S.D.	5.0	10.0	13.9	13.6	13.9	6.3	15.1	12.4	14.0	11.4	18.4	13.0
N	10	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

* Successive periods

** Food was weighed in on Day -6

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 1-F
DOSE: 0 (mg/kg)

SEX: FEMALE

ANIMAL # DAY 84 DAY 87

311	160	69
312	138	70
313	165	92
314	166	67
315	129	59
316	133	59
317	154	89
318	161	65
319	152	66
320	130	65

MEAN	149	70
S.D.	14.8	11.4
N	10	10

--: Data Unavailable

*Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL FOOD CONSUMPTION (Grams) *

STUDY: 107

GROUP: 2-F
DOSE: 0.5 (mg/kg)

SEX: FEMALE

ANIMAL #	DAY 0 **	DAY 7	DAY 14	DAY 21	DAY 28	DAY 31	DAY 43	DAY 49	DAY 56	DAY 59	DAY 70	DAY 77
331	125	173	179	178	193	82	212	154	191	83	185	182
332	113	134	144	132	143	64	154	102	139	73	154	130
333	111	130	159	154	161	78	192	151	168	77	188	167
334	124	137	154	147	149	68	186	138	162	72	173	157
335	121	164	169	156	175	93	202	170	182	83	190	172
336	117	147	174	164	196	76	185	144	183	83	170	169
337	121	158	160	145	159	77	167	138	179	87	162	153
338	122	148	149	144	147	76	169	144	162	77	159	145
339	99	128	132	120	125	78	169	105	139	64	154	132
340	125	132	143	157	147	62	179	119	169	71	159	155
MEAN	118	145	156	150	160	75	182	137	167	77	169	156
S.D.	8.2	15.6	14.9	16.2	22.6	9.0	17.6	21.7	17.7	7.1	14.0	17.0
N	10	10	10	10	10	10	10	10	10	10	10	10

---: Data Unavailable

* Successive periods

** Food was weighed in on Day -6

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

0 0 0 0 0

INDIVIDUAL FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 2-F
DOSE: 0.5 (mg/kg)
ANIMAL # DAY 84 DAY 87

SEX: FEMALE

331	183	88
332	138	56
333	164	78
334	149	74
335	166	81
336	165	74
337	148	68
338	163	63
339	125	60
340	165	69

MEAN	157	71
S.D.	16.7	9.9
N	10	10

--: Data Unavailable

*Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL FOOD CONSUMPTION (Grams) *

STUDY: 107

GROUP: 3-F

SEX: FEMALE

DOSE: 1.5 (mg/kg)

ANIMAL #	DAY 0 **	DAY 7	DAY 14	DAY 21	DAY 28	DAY 31	DAY 43	DAY 49	DAY 56	DAY 59	DAY 70	DAY 77
351	103	130	137	134	137	67	146	106	135	73	142	129
352	108	124	138	129	133	73	153	95	137	73	167	144
353	117	160	161	144	157	85	193	124	168	78	166	159
354	120	143	151	146	142	73	181	141	168	78	185	165
355	109	117	149	160	174	68	173	138	164	77	188	160
356	117	150	153	143	149	69	196	111	154	81	168	154
357	119	140	148	154	153	86	172	112	149	94	187	129
358	114	128	156	151	145	64	185	127	167	114	185	169
359	116	152	161	151	163	64	167	103	155	64	178	145
360	130	155	163	165	166	84	204	144	175	76	211	209
MEAN	115	140	152	148	152	73	177	120	157	81	178	156
S.D.	7.5	14.6	9.1	11.0	13.2	8.6	18.6	17.2	13.6	13.9	18.3	23.1
N	10	10	10	10	10	10	10	10	10	10	10	10

--: Data Unavailable

* Successive periods

** Food was weighed in on Day -6

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 3-F

SEX: FEMALE

DOSE: 1.5 (mg/kg)

ANIMAL # DAY 84 DAY 87

351	138	58
352	151	65
353	163	75
354	156	65
355	153	64
356	148	59
357	138	64
358	189	60
359	142	58
360	204	87

MEAN	158	66
S.D.	21.9	9.1
N	10	10

--: Data Unavailable

*Successive periods

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

000000

INDIVIDUAL FOOD CONSUMPTION (Grams)*

STUDY: 107

GROUP: 4-F

SEX: FEMALE

DOSE: 4.5 (mg/kg)

ANIMAL #	DAY 0**	DAY 7	DAY 14	DAY 21	DAY 28	DAY 31	DAY 43	DAY 49	DAY 56	DAY 59	DAY 70	DAY 77
371	127	153	153	142	162	73	185	129	145	67	184	155
372	120	147	131	137	141	105	182	124	152	98	191	179
373	108	129	138	122	130	69	151	109	138	67	153	138
374	106	130	122	119	118	59	162	100	154	69	143	132
375	131	156	150	140	143	68	194	121	134	76	157	172
376	108	128	105	109	110	71	140	89	127	51	138	125
377	116	148	128	117	120	57	141	103	121	67	147	145
378	111	136	131	123	138	64	147	131	136	62	153	148
379	107	145	148	114	136	77	184	149	156	71	177	158
380	107	138	127	107	128	68	170	112	151	58	183	148
MEAN	114	141	133	123	133	71	166	117	141	69	163	150
S.D.	9.1	10.2	14.6	12.6	14.9	13.4	20.1	17.6	12.1	12.5	19.3	16.8
N	10	10	10	10	10	10	10	10	10	10	10	10

---: Data Unavailable

* Successive periods

** Food was weighed in on Day -6

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL FOOD CONSUMPTION (Grams) *

STUDY: 107

GROUP: 4-F

SEX: FEMALE

DOSE: 4.5 (mg/kg)

ANIMAL # DAY 84 DAY 87

371	156	64
372	165	73
373	140	52
374	148	59
375	185	73
376	109	45
377	149	53
378	147	58
379	219	62
380	166	64

MEAN	158	60
S.D.	29.0	8.9
N	10	10

--: Data Unavailable

*Successive periods

100-100000

APPENDIX 6

Individual Clinical Chemistry Data

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Alanine Aminotransferase

STUDY ID: 107
STUDY NO: 107
ABBR: ALT

SEX: MALE

UNITS: U/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	67	64	53
302	58	44	47
303	54	58	50
304	59	61	56
305	61	71	54
306	74	57	55
307	58	52	40
308	59	56	53
309	60	49	44
310	74	69	64

MEAN	62	58	52
SD	6.9	8.5	6.8
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	56	49	47
322	65	56	53
323	53	56	52
324	66	54	51
325	65	68	61
326	60	63	56
327	70	45	43
328	55	51	63
329	63	64	59
330	66	61	55

MEAN	62	57	54
SD	5.6	7.3	6.2
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Alanine Aminotransferase

STUDY ID: 107
STUDY NO: 107
ABBR: ALT

SEX: MALE

UNITS: U/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	55	67	77
342	60	72	71
343	95	78	82
344	61	70	61
345	56	76	56
346	81	91	79
347	69	61	52
348	74	82	65
349	79	68	63
350	83	73	75

MEAN	71	74	68
SD	13.3	8.5	10.2
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	185	227	190
363	--	--	--
364	143	225	208
365	170	150	158
366	--	--	--
367	217	194	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	179	199	185
SD	30.9	36.0	25.3
N	4	4	3

(--)-Data Unavailable

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Sorbitol Dehydrogenase

STUDY ID: 107
STUDY NO: 107
ABBR: SDH

SEX: MALE

UNITS: U/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	11.7	17.9	13.3
302	14.1	12.9	14.7
303	11.9	6.3	11.8
304	16.4	20.0	17.5
305	17.6	11.7	17.6
306	14.9	8.8	15.7
307	17.6	14.4	11.5
308	18.1	13.1	20.9
309	20.1	11.0	12.8
310	11.5	21.6	11.3

MEAN	15.4	13.8	14.7
SD	3.04	4.84	3.19
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	15.6	11.8	10.9
322	15.8	14.0	14.3
323	10.3	12.0	17.2
324	20.0	12.5	16.5
325	19.8	13.9	7.5
326	11.0	14.0	16.0
327	14.2	15.0	14.0
328	7.9	12.2	19.6
329	7.8	5.4	14.1
330	15.5	14.1	22.4

MEAN	13.8	12.5	15.3
SD	4.42	2.72	4.20
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Sorbitol Dehydrogenase

STUDY ID: 107

SEX: MALE

STUDY NO: 107

ABBR: SDH

UNITS: U/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	15.0	15.6	22.6
342	17.8	17.7	21.1
343	13.6	15.0	20.1
344	14.3	20.0	18.6
345	17.2	11.1	10.5
346	13.1	18.3	22.6
347	33.8	16.7	9.5
348	20.5	21.1	24.2
349	13.8	14.4	12.6
350	20.5	17.9	22.5

MEAN	18.0	16.8	18.4
SD	6.20	2.90	5.49
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	23.2	30.0	49.2
363	--	--	--
364	QNS	10.5	23.9
365	38.9	27.3	45.3
366	--	--	--
367	28.5	19.4	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	30.2	21.8	39.5
SD	7.99	8.77	13.62
N	3	4	3

(--)-Data Unavailable

QNS-Quantity Not Sufficient

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Total ProteinSTUDY ID: 107
STUDY NO: 107
ABBR: TP

SEX: MALE

UNITS: g/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	7.7	8.1	8.4
302	7.3	7.1	7.4
303	8.0	7.4	7.0
304	8.4	8.5	7.7
305	8.3	8.4	8.2
306	7.7	7.4	7.8
307	7.5	8.4	7.3
308	7.7	7.9	8.6
309	8.3	7.9	8.2
310	7.9	8.1	8.0

MEAN	7.9	7.9	7.9
SD	0.37	0.48	0.51
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	7.3	7.7	7.9
322	6.8	7.5	7.1
323	7.4	7.2	8.3
324	7.3	6.8	7.6
325	7.8	8.0	7.7
326	7.6	8.2	7.7
327	7.9	8.1	8.0
328	7.8	7.2	7.9
329	8.0	7.6	7.9
330	8.1	7.8	7.7

MEAN	7.6	7.6	7.8
SD	0.40	0.45	0.31
N	10	10	10

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Total ProteinSTUDY ID: 107
STUDY NO: 107
ABBR: TP

SEX: MALE

UNITS: g/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	7.4	8.1	7.9
342	8.0	8.3	7.2
343	6.6	7.5	7.4
344	7.8	8.1	7.3
345	7.5	8.3	8.4
346	7.7	8.8	8.4
347	7.6	7.7	7.3
348	7.3	7.9	7.3
349	6.9	8.3	8.0
350	8.4	7.7	8.0

MEAN	7.5	8.1	7.7
SD	0.52	0.38	0.47
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	7.8	6.5	5.9
363	--	--	--
364	9.0	6.5	7.7
365	7.6	7.4	7.9
366	--	--	--
367	6.9	6.4	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	7.8	6.7	7.2
SD	0.87	0.47	1.10
N	4	4	3

(---)-Data Unavailable

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: AlbuminSTUDY ID: 107
STUDY NO: 107
ABBR: ALB

SEX: MALE

UNITS: g/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	4.5	4.1	4.4
302	4.0	3.9	4.2
303	4.2	4.2	3.7
304	5.1	4.4	3.9
305	4.4	4.4	4.3
306	4.2	4.3	4.2
307	4.3	4.7	4.0
308	4.3	4.0	4.5
309	4.7	4.5	4.2
310	4.7	4.2	4.3

MEAN	4.4	4.3	4.2
SD	0.32	0.24	0.24
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	3.8	4.3	4.0
322	3.8	3.8	4.0
323	4.4	4.2	4.5
324	3.9	4.0	4.1
325	4.3	4.6	4.4
326	4.2	4.9	4.4
327	4.5	4.2	4.0
328	4.2	3.8	4.3
329	4.3	4.1	4.2
330	5.9	4.0	4.1

MEAN	4.3	4.2	4.2
SD	0.60	0.34	0.19
N	10	10	10

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: AlbuminSTUDY ID: 107
STUDY NO: 107
ABBR: ALB

SEX: MALE

UNITS: g/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	4.2	4.3	4.4
342	4.9	4.4	3.4
343	3.8	4.0	4.1
344	4.2	4.5	4.1
345	4.0	4.4	4.4
346	4.1	4.7	4.4
347	4.2	4.5	4.1
348	4.0	5.4	4.2
349	3.7	4.1	4.4
350	5.5	4.2	4.2

MEAN	4.3	4.5	4.2
SD	0.54	0.39	0.30
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	4.4	3.3	3.4
363	--	--	--
364	4.9	3.6	4.3
365	4.5	4.8	4.4
366	--	--	--
367	4.6	3.4	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	4.6	3.8	4.0
SD	0.22	0.69	0.55
N	4	4	3

(--) - Data Unavailable

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: GlobulinSTUDY ID: 107
STUDY NO: 107
ABBR: GLOB

SEX: MALE

UNITS: g/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	3.2	4.0	4.0
302	3.3	3.2	3.2
303	3.8	3.2	3.3
304	3.3	4.1	3.8
305	3.9	4.0	3.9
306	3.5	3.1	3.6
307	3.2	3.7	3.3
308	3.4	3.9	4.1
309	3.6	3.4	4.0
310	3.2	3.9	3.7

MEAN	3.4	3.7	3.7
SD	0.25	0.39	0.33
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	3.5	3.4	3.9
322	3.0	3.7	3.1
323	3.0	3.0	3.8
324	3.4	2.8	3.5
325	3.5	3.4	3.3
326	3.4	3.3	3.3
327	3.4	3.9	4.0
328	3.6	3.4	3.6
329	3.7	3.5	3.7
330	2.2	3.8	3.6

MEAN	3.3	3.4	3.6
SD	0.44	0.34	0.29
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Globulin

STUDY ID: 107
STUDY NO: 107
ABBR: GLOB

SEX: MALE

UNITS: g/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	3.2	3.8	3.5
342	3.1	3.9	3.8
343	2.8	3.5	3.3
344	3.6	3.6	3.2
345	3.5	3.9	4.0
346	3.6	4.1	4.0
347	3.4	3.2	3.2
348	3.3	2.5	3.1
349	3.2	4.2	3.6
350	2.9	3.5	3.8

MEAN	3.3	3.6	3.6
SD	0.28	0.50	0.34
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	3.4	3.2	2.5
363	--	--	--
364	4.1	2.9	3.4
365	3.1	2.6	3.5
366	--	--	--
367	2.3	3.0	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	3.2	2.9	3.1
SD	0.75	0.25	0.55
N	4	4	3

(--)-Data Unavailable

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: A/G RatioSTUDY ID: 107
STUDY NO: 107
ABBR: A/G

SEX: MALE

UNITS: -

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	1.41	1.03	1.10
302	1.21	1.22	1.31
303	1.11	1.31	1.12
304	1.55	1.07	1.03
305	1.13	1.10	1.10
306	1.20	1.39	1.17
307	1.34	1.27	1.21
308	1.26	1.03	1.10
309	1.31	1.32	1.05
310	1.47	1.08	1.16

MEAN	1.30	1.18	1.14
SD	0.145	0.135	0.082
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	1.09	1.26	1.03
322	1.27	1.03	1.29
323	1.47	1.40	1.18
324	1.15	1.43	1.17
325	1.23	1.35	1.33
326	1.24	1.48	1.33
327	1.32	1.08	1.00
328	1.17	1.12	1.19
329	1.16	1.17	1.14
330	2.68	1.05	1.14

MEAN	1.38	1.24	1.18
SD	0.470	0.169	0.113
N	10	10	10

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: A/G Ratio

STUDY ID: 107
STUDY NO: 107
ABBR: A/G

SEX: MALE

UNITS: -

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	1.31	1.13	1.26
342	1.58	1.13	0.89
343	1.36	1.14	1.24
344	1.17	1.25	1.28
345	1.14	1.13	1.10
346	1.14	1.15	1.10
347	1.24	1.41	1.28
348	1.21	2.16	1.35
349	1.16	0.98	1.22
350	1.90	1.20	1.11

MEAN	1.32	1.27	1.18
SD	0.244	0.332	0.134
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	1.29	1.03	1.36
363	--	--	--
364	1.20	1.24	1.26
365	1.45	1.85	1.26
366	--	--	--
367	2.00	1.13	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	1.49	1.31	1.29
SD	0.359	0.368	0.058
N	4	4	3

(--)-Data Unavailable

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Total Bile AcidsSTUDY ID: 107
STUDY NO: 107
ABBR: TBA

SEX: MALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	44.4	55.8	72.1
302	35.3	41.2	54.2
303	24.5	37.3	25.5
304	36.8	27.7	22.6
305	41.3	68.0	65.6
306	52.9	33.6	30.1
307	58.6	86.0	50.3
308	81.5	47.3	80.4
309	30.9	44.0	30.0
310	30.0	47.3	21.3

MEAN	43.6	48.8	45.2
SD	16.93	17.31	22.15
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	65.0	52.8	9.9
322	25.9	25.4	19.9
323	30.9	37.2	56.0
324	74.3	17.6	32.0
325	25.0	45.0	42.4
326	45.4	27.1	39.1
327	44.3	23.0	29.3
328	30.1	44.2	79.1
329	62.3	47.5	98.5
330	32.4	26.4	24.4

MEAN	43.6	34.6	43.1
SD	17.90	12.19	27.59
N	10	10	10

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Total Bile AcidsSTUDY ID: 107
STUDY NO: 107
ABBR: TBA

SEX: MALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	45.2	45.4	95.8
342	83.3	68.6	34.5
343	33.4	42.4	91.8
344	30.3	25.0	18.1
345	36.7	39.2	34.5
346	52.7	52.3	29.4
347	21.5	113.4	45.3
348	17.5	107.4	97.9
349	57.7	34.1	114.0
350	23.1	67.1	37.3

MEAN	40.1	59.5	59.9
SD	20.16	30.06	35.54
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	285.9	139.9	147.7
363	--	--	--
364	160.0	383.8	144.8
365	444.6	299.9	383.6
366	--	--	--
367	120.5	48.7	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	252.8	218.1	225.4
SD	146.06	151.61	137.04
N	4	4	3

(---)-Data Unavailable

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Alkaline PhosphataseSTUDY ID: 107
STUDY NO: 107
ABBR: ALKP

SEX: MALE

UNITS: U/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	277	198	172
302	176	129	123
303	263	160	130
304	280	239	157
305	242	200	200
306	255	141	138
307	218	235	126
308	282	195	156
309	189	119	91
310	216	140	121

MEAN	240	176	141
SD	38.4	43.6	30.7
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	222	156	137
322	180	138	110
323	271	272	179
324	216	151	141
325	336	312	227
326	421	377	194
327	280	162	130
328	178	129	140
329	298	221	210
330	189	126	103

MEAN	259	204	157
SD	78.3	87.8	42.6
N	10	10	10

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Alkaline PhosphataseSTUDY ID: 107
STUDY NO: 107
ABBR: ALKP

SEX: MALE

UNITS: U/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	278	175	207
342	206	154	164
343	305	226	174
344	211	184	120
345	273	243	169
346	268	211	196
347	233	190	147
348	226	282	160
349	209	186	168
350	195	137	108

MEAN	240	199	161
SD	37.7	43.0	30.4
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	291	294	145
363	--	--	--
364	364	393	288
365	258	205	204
366	--	--	--
367	284	279	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	299	293	212
SD	45.4	77.3	71.9
N	4	4	3

(--) - Data Unavailable

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: CholesterolSTUDY ID: 107
STUDY NO: 107
ABBR: CHOL

SEX: MALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	39	40	57
302	48	49	51
303	52	47	44
304	75	83	89
305	51	35	52
306	60	45	58
307	46	49	49
308	49	45	59
309	50	51	74
310	43	37	51

MEAN	51	48	58
SD	10.0	13.4	13.5
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	57	48	62
322	56	53	56
323	58	53	61
324	39	33	41
325	47	49	58
326	90	106	73
327	77	65	77
328	57	37	48
329	38	40	49
330	49	38	46

MEAN	57	52	57
SD	16.1	21.2	11.6
N	10	10	10

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: CholesterolSTUDY ID: 107
STUDY NO: 107
ABBR: CHOL

SEX: MALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	60	61	53
342	53	57	63
343	71	53	57
344	47	55	57
345	55	54	69
346	67	74	79
347	59	57	59
348	49	49	54
349	42	61	61
350	55	48	58

MEAN	56	57	61
SD	8.9	7.4	7.8
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	73	127	139
363	--	--	--
364	85	97	111
365	86	74	74
366	--	--	--
367	106	102	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	88	100	108
SD	13.7	21.7	32.6
N	4	4	3

(--) - Data Unavailable

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Triglycerides

STUDY ID: 107

SEX: MALE

STUDY NO: 107

ABBR: TRY

UNITS: mg/dL

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 1-M:0 mg base/kg/day

301	118	173	262
302	62	129	122
303	87	97	55
304	119	194	324
305	12	60	87
306	213	148	200
307	50	109	41
308	78	83	105
309	126	116	228
310	61	60	111

MEAN	93	117	154
SD	55.2	45.1	94.6
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	40	31	59
322	69	117	119
323	100	187	219
324	44	97	110
325	141	171	192
326	184	179	239
327	78	105	102
328	62	51	81
329	74	135	133
330	112	110	152

MEAN	90	118	141
SD	45.0	52.0	59.4
N	10	10	10

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: TriglyceridesSTUDY ID: 107
STUDY NO: 107
ABBR: TRY

SEX: MALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	55	92	68
342	80	100	92
343	29	87	88
344	60	72	73
345	73	111	138
346	63	109	111
347	45	78	77
348	30	56	75
349	52	115	96
350	94	75	92

MEAN	58	90	91
SD	20.7	19.4	20.9
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	49	89	97
363	--	--	--
364	66	144	103
365	69	76	54
366	--	--	--
367	104	116	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	72	106	85
SD	23.1	30.2	26.7
N	4	4	3

(--) - Data Unavailable

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Blood Urea Nitrogen

STUDY ID: 107
STUDY NO: 107
ABBR: BUN

SEX: MALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	17.8	18.6	14.8
302	14.4	13.4	15.1
303	11.5	14.2	12.9
304	13.4	15.3	15.3
305	11.9	15.0	17.0
306	23.9	20.9	21.7
307	14.2	21.3	16.7
308	15.5	19.9	21.3
309	13.3	20.9	17.1
310	10.6	14.0	15.7

MEAN	14.7	17.4	16.8
SD	3.85	3.25	2.79
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	16.7	15.0	13.9
322	10.7	14.1	15.0
323	13.4	16.7	17.3
324	20.6	19.5	17.7
325	14.8	16.4	14.9
326	17.9	14.8	17.6
327	10.4	11.9	16.0
328	12.1	14.1	23.7
329	15.6	11.9	18.9
330	14.8	16.4	13.9

MEAN	14.7	15.1	16.9
SD	3.21	2.31	2.94
N	10	10	10

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Blood Urea NitrogenSTUDY ID: 107
STUDY NO: 107
ABBR: BUN

SEX: MALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	11.0	13.1	14.9
342	18.4	19.3	23.8
343	15.1	16.3	15.9
344	15.9	17.6	17.0
345	13.3	15.1	15.4
346	19.1	17.6	17.0
347	17.9	18.4	17.4
348	13.6	20.7	18.7
349	19.3	16.3	17.8
350	14.7	17.3	12.6

MEAN	15.8	17.2	17.1
SD	2.79	2.14	2.93
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	26.8	19.2	25.9
363	--	--	--
364	24.3	18.1	19.4
365	19.3	21.9	22.5
366	--	--	--
367	16.2	29.9	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	21.7	22.3	22.6
SD	4.79	5.33	3.25
N	4	4	3

(--) - Data Unavailable

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: CreatinineSTUDY ID: 107
STUDY NO: 107
ABBR: CREA

SEX: MALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	0.52	0.47	0.52
302	0.54	0.52	0.59
303	0.50	0.54	0.51
304	0.54	0.51	0.58
305	0.49	0.55	0.48
306	0.51	0.57	0.61
307	0.48	0.58	0.55
308	0.57	0.57	0.50
309	0.57	0.55	0.48
310	0.54	0.56	0.54

MEAN	0.53	0.54	0.54
SD	0.031	0.034	0.046
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	0.46	0.55	0.56
322	0.60	0.68	0.63
323	0.50	0.44	0.47
324	0.55	0.53	0.56
325	0.49	0.58	0.52
326	0.46	0.57	0.50
327	0.58	0.64	0.58
328	0.49	0.59	0.64
329	0.51	0.51	0.52
330	0.52	0.55	0.56

MEAN	0.52	0.56	0.55
SD	0.047	0.067	0.054
N	10	10	10

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: CreatinineSTUDY ID: 107
STUDY NO: 107
ABBR: CREA

SEX: MALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	0.52	0.56	0.56
342	0.60	0.55	0.56
343	0.47	0.55	0.66
344	0.59	0.60	0.59
345	0.54	0.60	0.49
346	0.54	0.61	0.58
347	0.54	0.63	0.65
348	0.61	0.67	0.56
349	0.54	0.62	0.66
350	0.61	0.51	0.54

MEAN	0.56	0.59	0.59
SD	0.046	0.047	0.056
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	0.48	0.54	0.80
363	--	--	--
364	0.66	0.50	0.65
365	0.55	0.60	0.73
366	--	--	--
367	0.78	0.74	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	0.62	0.60	0.73
SD	0.131	0.105	0.075
N	4	4	3

(--)Data Unavailable

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Sodium

STUDY ID: 107

SEX: MALE

STUDY NO: 107

ABBR: NA

UNITS: mmol/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	146	142	147
302	144	142	145
303	145	143	144
304	143	145	144
305	144	143	144
306	145	145	147
307	143	145	142
308	146	142	148
309	144	144	143
310	145	146	144
MEAN	145	144	145
SD	1.1	1.5	1.9
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	144	142	144
322	143	144	143
323	141	143	142
324	142	140	143
325	144	146	145
326	144	144	147
327	144	147	147
328	143	142	151
329	143	142	143
330	146	146	146
MEAN	143	144	145
SD	1.3	2.2	2.7
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Sodium

STUDY ID: 107
STUDY NO: 107
ABBR: NA

SEX: MALE

UNITS: mmol/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	141	145	146
342	146	144	145
343	145	143	145
344	144	146	145
345	144	144	147
346	142	144	146
347	143	145	146
348	145	143	143
349	141	146	145
350	146	144	146

MEAN	144	144	145
SD	1.9	1.1	1.1
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	142	142	149
363	--	--	--
364	148	142	146
365	146	141	143
366	--	--	--
367	146	144	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	146	142	146
SD	2.5	1.3	3.0
N	4	4	3

(--)-Data Unavailable

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

BBAT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Potassium

STUDY ID: 107
STUDY NO: 107
ABBR: K

SEX: MALE

UNITS: mmol/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	5.57	5.57	5.40
302	5.06	5.78	5.68
303	5.62	5.42	6.02
304	5.98	5.61	4.77
305	5.53	6.10	5.96
306	5.85	6.03	5.31
307	5.82	6.35	6.12
308	5.23	5.70	4.87
309	5.99	6.88	5.94
310	5.68	5.94	6.75

MEAN	5.63	5.94	5.68
SD	0.305	0.433	0.605
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	5.68	4.81	5.70
322	5.72	5.60	5.64
323	5.29	6.15	5.76
324	6.27	5.49	6.22
325	5.56	5.35	5.54
326	5.32	5.34	5.77
327	6.16	5.88	5.60
328	5.16	6.66	7.84
329	4.98	5.29	5.79
330	6.43	5.93	5.91

MEAN	5.66	5.65	5.98
SD	0.494	0.522	0.682
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Potassium

STUDY ID: 107
STUDY NO: 107
ABBR: K

SEX: MALE

UNITS: mmol/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	5.88	5.99	6.03
342	5.71	5.82	4.80
343	5.04	6.38	5.60
344	5.77	6.26	5.53
345	5.53	5.08	5.16
346	5.86	6.38	5.31
347	5.95	5.81	5.62
348	5.37	5.44	5.65
349	5.35	5.25	5.48
350	4.96	5.11	5.05

MEAN	5.54	5.75	5.42
SD	0.353	0.508	0.352
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	6.43	5.89	7.35
363	--	--	--
364	7.34	5.30	5.62
365	5.83	5.33	6.51
366	--	--	--
367	5.45	6.19	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	6.26	5.68	6.49
SD	0.824	0.436	0.865
N	4	4	3

(--)-Data Unavailable

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Chloride

STUDY ID: 107
STUDY NO: 107
ABBR: CL

SEX: MALE

UNITS: mEq/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	116	117	116
302	118	115	116
303	123	113	114
304	122	120	114
305	113	118	116
306	106	112	115
307	112	119	119
308	113	117	119
309	126	116	117
310	122	115	112
MEAN	117	116	116
SD	6.2	2.5	2.2
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	113	117	113
322	108	113	115
323	110	110	124
324	116	110	115
325	104	108	108
326	110	112	109
327	114	113	111
328	112	113	116
329	111	113	120
330	116	110	115
MEAN	111	112	115
SD	3.7	2.5	4.8
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

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INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Chloride

STUDY ID: 107
STUDY NO: 107
ABBR: CL

SEX: MALE

UNITS: mEq/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	113	111	120
342	120	127	110
343	109	121	120
344	123	123	112
345	112	119	125
346	108	107	112
347	109	110	113
348	112	111	117
349	116	122	117
350	128	118	115

MEAN	115	117	116
SD	6.7	6.7	4.6
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	113	123	104
363	--	--	--
364	118	108	120
365	109	119	125
366	--	--	--
367	119	120	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	115	118	116
SD	4.6	6.6	11.0
N	4	4	3

(--)-Data Unavailable

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Calcium

STUDY ID: 107
STUDY NO: 107
ABBR: CA

SEX: MALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	11.3	11.4	11.9
302	11.1	11.1	9.6
303	10.5	11.3	10.2
304	11.3	9.7	10.9
305	13.9	12.1	10.7
306	11.1	10.9	10.6
307	11.1	10.9	10.9
308	11.4	10.5	11.8
309	10.5	11.2	11.5
310	11.2	12.0	11.3

MEAN	11.3	11.1	10.9
SD	0.95	0.70	0.72
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	10.5	10.4	10.6
322	10.5	11.2	10.4
323	11.1	10.1	12.0
324	10.6	10.1	10.4
325	11.0	11.3	11.0
326	11.5	11.3	11.2
327	10.7	11.6	11.3
328	10.6	10.9	12.9
329	11.3	11.6	10.6
330	11.4	11.6	10.8

MEAN	10.9	11.0	11.1
SD	0.39	0.60	0.79
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Calcium

STUDY ID: 107
STUDY NO: 107
ABBR: CA

SEX: MALE

UNITS: mg/dL

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 3-M:1.5 mg base/kg/day

341	11.2	11.1	11.0
342	11.5	10.9	11.4
343	10.5	10.7	11.1
344	11.1	9.8	11.0
345	11.2	10.8	11.8
346	11.0	10.1	11.4
347	11.0	11.4	10.8
348	10.8	10.2	10.5
349	10.2	10.8	11.6
350	11.1	10.5	11.2

MEAN	11.0	10.6	11.2
SD	0.37	0.49	0.39
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	11.4	11.1	11.3
363	--	--	--
364	12.9	11.1	11.4
365	11.4	10.9	11.7
366	--	--	--
367	11.6	11.2	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	11.8	11.1	11.5
SD	0.72	0.13	0.21
N	4	4	3

(--)-Data Unavailable

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Inorganic Phosphorus

STUDY ID: 107
STUDY NO: 107
ABBR: IP

SEX: MALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	10.7	10.6	8.4
302	9.4	8.9	8.7
303	10.4	8.1	8.7
304	11.6	9.2	8.5
305	9.1	11.2	9.8
306	10.2	9.3	8.7
307	10.7	8.1	10.3
308	9.9	9.3	8.6
309	11.2	10.5	9.6
310	10.2	9.4	9.4

MEAN	10.3	9.5	9.1
SD	0.76	1.03	0.65
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	10.5	8.7	7.3
322	8.5	8.3	8.2
323	9.5	9.8	10.3
324	11.4	9.9	8.9
325	9.5	9.0	9.4
326	11.6	7.6	8.1
327	9.4	9.4	7.9
328	8.2	9.4	15.8
329	9.5	9.3	9.9
330	9.8	7.8	9.8

MEAN	9.8	8.9	9.6
SD	1.10	0.80	2.40
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Inorganic Phosphorus

STUDY ID: 107
STUDY NO: 107
ABBR: IP

SEX: MALE

UNITS: mg/dL

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 3-M:1.5 mg base/kg/day

341	9.9	7.9	8.6
342	10.7	10.0	7.9
343	8.5	10.0	11.3
344	11.8	10.4	7.3
345	9.6	8.8	8.3
346	10.6	10.5	7.9
347	10.6	9.5	8.6
348	8.5	8.3	9.0
349	10.0	9.2	8.9
350	9.9	8.1	7.7

MEAN	10.0	9.3	8.6
SD	1.01	0.96	1.11
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	11.1	11.4	7.3
363	--	--	--
364	12.0	7.9	8.7
365	9.1	9.3	10.8
366	--	--	--
367	10.4	7.8	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	10.7	9.1	8.9
SD	1.22	1.68	1.76
N	4	4	3

(--)-Data Unavailable

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Glucose

STUDY ID: 107
STUDY NO: 107
ABBR: GLU

SEX: MALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	131	185	159
302	142	127	137
303	145	120	134
304	206	163	250
305	121	183	147
306	146	164	154
307	124	142	164
308	180	129	198
309	167	147	156
310	164	232	141

MEAN	153	159	164
SD	26.7	34.2	35.3
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	116	178	132
322	115	115	148
323	148	156	216
324	185	196	153
325	136	136	152
326	190	137	145
327	139	118	137
328	136	134	190
329	152	129	216
330	152	121	129

MEAN	147	142	162
SD	25.0	26.8	33.2
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

38AET

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Glucose

STUDY ID: 107
STUDY NO: 107
ABBR: GLU

SEX: MALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	129	130	136
342	134	140	168
343	141	132	178
344	179	154	131
345	121	126	139
346	131	171	149
347	133	121	133
348	142	124	162
349	142	151	147
350	184	138	134

MEAN	144	139	148
SD	21.0	15.8	16.4
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	124	108	84
363	--	--	--
364	145	96	126
365	115	129	120
366	--	--	--
367	113	115	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	124	112	110
SD	14.6	13.8	22.7
N	4	4	3

(--)-Data Unavailable

LABCAT CC4.25

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THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Alanine Aminotransferase

STUDY ID: 107
STUDY NO: 107
ABBR: ALT

SEX: FEMALE

UNITS: U/L

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 1-F:0 mg base/kg/day

311	83	67	84
312	64	70	60
313	64	45	52
314	55	70	53
315	84	76	61
316	71	46	47
317	90	98	88
318	54	38	38
319	59	56	36
320	47	36	37

MEAN	67	60	56
SD	14.5	19.6	18.4
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	51	49	39
332	64	78	124
333	49	57	79
334	69	51	63
335	70	49	60
336	52	54	68
337	49	58	50
338	78	69	56
339	67	47	72
340	72	56	73

MEAN	62	57	68
SD	10.8	9.8	22.8
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Alanine Aminotransferase

STUDY ID: 107
STUDY NO: 107
ABBR: ALT

SEX: FEMALE

UNITS: U/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	86	56	89
352	48	43	37
353	52	43	39
354	92	62	97
355	57	42	45
356	70	60	72
357	63	64	72
358	75	55	66
359	52	53	53
360	69	49	52

MEAN	66	53	62
SD	14.9	8.2	20.5
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	90	55	50
372	90	103	62
373	87	68	59
374	53	51	46
375	67	73	62
376	52	53	60
377	81	67	62
378	67	52	61
379	85	57	62
380	72	58	49

MEAN	74	64	57
SD	14.4	15.7	6.3
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Sorbitol Dehydrogenase

STUDY ID: 107
STUDY NO: 107
ABBR: SDH

SEX: FEMALE

UNITS: U/L

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 1-F:0 mg base/kg/day

311	3.2	9.4	13.3
312	18.4	13.0	12.3
313	16.3	6.8	17.7
314	12.4	20.3	11.2
315	16.3	13.7	15.1
316	17.4	2.3	15.1
317	18.2	18.7	27.0
318	4.9	11.0	11.6
319	16.1	15.9	12.3
320	13.6	1.6	7.9

MEAN	13.7	11.3	14.4
SD	5.42	6.36	5.17
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	16.1	17.3	10.1
332	16.2	15.6	24.0
333	13.9	19.9	19.2
334	25.3	16.8	21.8
335	10.1	32.8	6.4
336	19.8	12.9	19.9
337	19.8	15.6	18.5
338	9.2	14.4	11.4
339	26.6	14.9	20.9
340	16.2	16.1	16.7

MEAN	17.3	17.6	16.9
SD	5.73	5.65	5.72
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Sorbitol Dehydrogenase

STUDY ID: 107
STUDY NO: 107
ABBR: SDH

SEX: FEMALE

UNITS: U/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	19.0	14.1	23.3
352	13.8	26.4	19.3
353	10.2	10.4	11.7
354	11.3	11.9	22.3
355	24.3	12.5	9.1
356	19.4	10.4	25.2
357	28.4	12.3	8.6
358	13.7	12.0	17.7
359	18.2	26.3	18.3
360	18.7	16.4	14.4

MEAN	17.7	15.3	17.0
SD	5.70	6.09	5.87
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	16.8	18.9	22.2
372	17.2	20.4	21.6
373	21.3	20.5	--
374	20.5	19.7	17.0
375	25.8	16.6	22.5
376	35.9	19.2	15.0
377	21.4	12.5	18.6
378	13.1	17.4	25.8
379	17.4	16.4	17.6
380	22.3	14.9	12.6

MEAN	21.2	17.7	19.2
SD	6.28	2.60	4.16
N	10	10	9

(--)-Data Unavailable

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Total Protein

STUDY ID: 107
STUDY NO: 107
ABBR: TP

SEX: FEMALE

UNITS: g/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	7.9	7.3	8.2
312	7.3	7.1	8.3
313	8.3	8.3	8.6
314	8.5	8.9	8.7
315	8.0	9.6	9.4
316	8.0	7.6	8.3
317	8.8	8.5	8.1
318	8.4	8.5	8.2
319	7.3	7.9	8.0
320	8.7	8.0	8.1

MEAN	8.1	8.2	8.4
SD	0.52	0.76	0.42
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	7.5	7.2	8.2
332	7.6	8.6	8.2
333	8.0	8.5	8.7
334	8.1	7.4	8.4
335	8.5	7.8	8.4
336	8.0	8.8	9.9
337	7.8	7.5	8.0
338	7.8	7.6	7.9
339	8.4	9.0	9.4
340	9.3	9.1	10.0

MEAN	8.1	8.2	8.7
SD	0.53	0.72	0.78
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Total Protein

STUDY ID: 107
STUDY NO: 107
ABBR: TP

SEX: FEMALE

UNITS: g/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	8.9	8.4	8.7
352	8.0	7.9	8.0
353	9.2	9.2	9.3
354	8.7	8.0	8.5
355	8.9	8.7	9.1
356	8.0	8.7	8.7
357	8.6	7.5	8.8
358	7.8	7.0	7.8
359	8.4	8.4	8.7
360	8.1	8.3	8.3

MEAN	8.5	8.2	8.6
SD	0.47	0.64	0.46
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	8.8	9.2	9.5
372	9.1	8.3	8.6
373	8.2	9.0	8.8
374	8.3	8.5	8.9
375	8.8	8.1	9.2
376	8.8	7.8	9.4
377	7.4	7.7	8.4
378	8.7	8.3	9.6
379	8.3	8.6	8.9
380	8.2	8.4	8.9

MEAN	8.5	8.4	9.0
SD	0.49	0.47	0.39
N	10	10	10

LABCAT CC4.25

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THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Albumin

STUDY ID: 107
STUDY NO: 107
ABBR: ALB

SEX: FEMALE

UNITS: g/dL

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 1-F:0 mg base/kg/day

311	4.2	4.3	4.9
312	4.1	4.4	4.5
313	4.6	5.2	4.4
314	4.7	5.0	4.8
315	4.5	6.6	5.2
316	5.1	4.3	4.6
317	5.1	5.0	4.6
318	4.4	4.6	4.9
319	3.9	4.2	4.2
320	5.5	4.3	4.5

MEAN	4.6	4.8	4.7
SD	0.50	0.73	0.29
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	4.2	4.5	4.6
332	4.3	4.8	4.6
333	4.2	4.6	4.9
334	4.3	4.6	4.8
335	4.2	4.4	4.4
336	4.2	5.0	5.6
337	4.7	5.3	4.7
338	4.1	4.4	4.4
339	5.2	5.7	5.8
340	5.8	5.1	5.8

MEAN	4.5	4.8	5.0
SD	0.56	0.43	0.56
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Albumin

STUDY ID: 107
STUDY NO: 107
ABBR: ALB

SEX: FEMALE

UNITS: g/dL

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 3-F:1.5 mg base/kg/day

351	5.5	4.8	4.9
352	4.8	4.6	4.7
353	4.9	5.3	5.2
354	5.1	5.2	4.8
355	5.2	5.0	5.0
356	4.3	5.1	4.5
357	4.7	4.7	4.8
358	4.4	4.2	4.2
359	4.7	4.6	5.4
360	4.2	4.4	4.8

MEAN	4.8	4.8	4.8
SD	0.41	0.36	0.34
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	5.1	4.9	5.4
372	4.9	5.8	4.7
373	5.1	4.9	5.5
374	5.1	5.0	5.7
375	4.7	5.4	5.2
376	4.6	4.9	5.1
377	4.2	4.3	4.6
378	4.9	4.9	5.4
379	4.5	4.8	5.2
380	4.3	4.9	4.8

MEAN	4.7	5.0	5.2
SD	0.33	0.39	0.36
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Globulin

STUDY ID: 107
STUDY NO: 107
ABBR: GLOB

SEX: FEMALE

UNITS: g/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	3.7	3.0	3.3
312	3.2	2.7	3.8
313	3.7	3.1	4.2
314	3.8	3.9	3.9
315	3.5	3.0	4.2
316	2.9	3.3	3.7
317	3.7	3.5	3.5
318	4.0	3.9	3.3
319	3.4	3.7	3.8
320	3.2	3.7	3.6

MEAN	3.5	3.4	3.7
SD	0.33	0.42	0.32
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	3.3	2.7	3.6
332	3.3	3.8	3.6
333	3.8	3.9	3.8
334	3.8	2.8	3.6
335	4.3	3.4	4.0
336	3.8	3.8	4.3
337	3.1	2.2	3.3
338	3.7	3.2	3.5
339	3.2	3.3	3.6
340	3.5	4.0	4.2

MEAN	3.6	3.3	3.8
SD	0.37	0.60	0.32
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Globulin

STUDY ID: 107
STUDY NO: 107
ABBR: GLOB

SEX: FEMALE

UNITS: g/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	3.4	3.6	3.8
352	3.2	3.3	3.3
353	4.3	3.9	4.1
354	3.6	2.8	3.7
355	3.7	3.7	4.1
356	3.7	3.6	4.2
357	3.9	2.8	4.0
358	3.4	2.8	3.6
359	3.7	3.8	3.3
360	3.9	3.9	3.5

MEAN	3.7	3.4	3.8
SD	0.31	0.46	0.33
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	3.7	4.3	4.1
372	4.2	2.5	3.9
373	3.1	4.1	3.3
374	3.2	3.5	3.2
375	4.1	2.7	4.0
376	4.2	2.9	4.3
377	3.2	3.4	3.8
378	3.8	3.4	4.2
379	3.8	3.8	3.7
380	3.9	3.5	4.1

MEAN	3.7	3.4	3.9
SD	0.42	0.58	0.37
N	10	10	10

LABCAT CC4.25

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THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: A/G Ratio

STUDY ID: 107
STUDY NO: 107
ABBR: A/G

SEX: FEMALE

UNITS: -

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	1.14	1.43	1.48
312	1.28	1.63	1.18
313	1.24	1.68	1.05
314	1.24	1.28	1.23
315	1.29	2.20	1.24
316	1.76	1.30	1.24
317	1.38	1.43	1.31
318	1.10	1.18	1.48
319	1.15	1.14	1.11
320	1.72	1.16	1.25

MEAN	1.33	1.44	1.26
SD	0.231	0.325	0.139
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	1.27	1.67	1.28
332	1.30	1.26	1.28
333	1.11	1.18	1.29
334	1.13	1.64	1.33
335	0.98	1.29	1.10
336	1.11	1.32	1.30
337	1.52	2.41	1.42
338	1.11	1.38	1.26
339	1.63	1.73	1.61
340	1.66	1.28	1.38

MEAN	1.28	1.52	1.33
SD	0.241	0.369	0.131
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: A/G Ratio

STUDY ID: 107
STUDY NO: 107
ABBR: A/G

SEX: FEMALE

UNITS: -

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	1.62	1.33	1.29
352	1.50	1.39	1.42
353	1.14	1.36	1.27
354	1.42	1.86	1.30
355	1.41	1.35	1.22
356	1.16	1.42	1.07
357	1.21	1.68	1.20
358	1.29	1.50	1.17
359	1.27	1.21	1.64
360	1.08	1.13	1.37

MEAN	1.31	1.42	1.30
SD	0.173	0.214	0.157
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	1.38	1.14	1.32
372	1.17	2.32	1.21
373	1.65	1.20	1.67
374	1.59	1.43	1.78
375	1.15	2.00	1.30
376	1.10	1.69	1.19
377	1.31	1.26	1.21
378	1.29	1.44	1.29
379	1.18	1.26	1.41
380	1.10	1.40	1.17

MEAN	1.29	1.51	1.36
SD	0.196	0.381	0.209
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

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INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Total Bile Acids

STUDY ID: 107
STUDY NO: 107
ABBR: TBA

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	28.3	30.6	32.1
312	29.2	21.5	34.0
313	62.0	32.7	44.2
314	38.5	20.2	24.5
315	25.9	85.8	61.6
316	45.4	13.2	12.1
317	15.5	29.6	43.7
318	11.1	16.7	20.7
319	35.9	13.9	19.2
320	56.7	27.8	10.7

MEAN	34.9	29.2	30.3
SD	16.44	21.10	16.10
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	66.4	32.5	20.4
332	20.4	20.0	33.3
333	55.5	71.2	26.7
334	97.1	35.3	34.4
335	126.5	32.5	28.3
336	35.1	25.1	31.8
337	15.1	32.4	24.8
338	17.3	17.2	34.1
339	19.7	21.4	59.5
340	24.7	53.0	40.4

MEAN	47.8	34.1	33.4
SD	38.39	16.57	10.79
N	10	10	10

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Total Bile AcidsSTUDY ID: 107
STUDY NO: 107
ABBR: TBA

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 3-F:1.5 mg base/kg/day

351	107.8	32.6	71.2
352	17.2	17.2	19.1
353	18.2	14.6	24.4
354	75.3	24.8	45.7
355	41.8	39.1	24.7
356	111.9	24.5	47.0
357	16.5	40.7	28.4
358	33.3	14.6	97.2
359	18.3	32.0	30.3
360	28.2	66.7	23.6

MEAN	46.9	30.7	41.2
SD	37.64	15.80	25.22
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	80.5	76.4	81.2
372	45.1	29.0	40.5
373	137.6	75.4	109.3
374	37.1	38.3	36.9
375	18.3	105.0	108.5
376	51.9	65.1	41.3
377	75.7	44.9	66.1
378	100.0	107.1	138.4
379	291.0	291.9	96.2
380	28.5	55.4	21.7

MEAN	86.6	88.9	74.0
SD	80.37	75.95	38.72
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Alkaline Phosphatase

STUDY ID: 107
STUDY NO: 107
ABBR: ALKP

SEX: FEMALE

UNITS: U/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	232	148	122
312	174	117	89
313	138	105	83
314	165	98	107
315	91	52	31
316	139	96	83
317	214	187	126
318	140	109	66
319	163	106	88
320	155	106	218

MEAN	161	112	101
SD	40.0	35.2	49.3
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	150	89	47
332	180	140	99
333	152	123	92
334	180	136	103
335	309	125	107
336	103	68	46
337	140	239	67
338	190	165	87
339	184	98	59
340	132	76	40

MEAN	172	126	75
SD	55.4	50.1	25.8
N	10	10	10

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Alkaline PhosphataseSTUDY ID: 107
STUDY NO: 107
ABBR: ALKP

SEX: FEMALE

UNITS: U/L

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 3-F:1.5 mg base/kg/day

351	201	122	78
352	157	113	86
353	169	72	57
354	259	144	118
355	110	81	71
356	122	120	56
357	220	168	105
358	116	140	69
359	140	52	58
360	123	88	58

MEAN	162	110	76
SD	50.3	36.2	21.6
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	213	110	116
372	236	152	78
373	266	111	98
374	171	127	99
375	178	105	110
376	189	57	38
377	119	90	72
378	212	103	65
379	260	142	100
380	167	124	87

MEAN	201	112	86
SD	45.5	26.9	23.5
N	10	10	10

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: CholesterolSTUDY ID: 107
STUDY NO: 107
ABBR: CHOL

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 1-F:0 mg base/kg/day

311	58	44	44
312	47	47	43
313	55	52	42
314	56	59	55
315	52	66	72
316	55	49	55
317	53	56	53
318	62	53	63
319	57	60	57
320	87	65	96

MEAN	58	55	58
SD	10.9	7.4	16.3
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	61	54	62
332	68	55	49
333	44	48	53
334	49	47	60
335	73	55	62
336	48	53	66
337	40	36	36
338	60	62	57
339	73	79	98
340	47	47	72

MEAN	56	54	62
SD	12.3	11.3	16.2
N	10	10	10

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Cholesterol

STUDY ID: 107
STUDY NO: 107
ABBR: CHOL

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	79	76	68
352	86	70	73
353	69	61	63
354	72	52	57
355	64	66	76
356	58	73	67
357	57	47	54
358	57	55	61
359	41	43	63
360	88	74	99

MEAN	67	62	68
SD	14.7	11.9	12.8
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	75	77	84
372	86	80	75
373	90	93	91
374	76	70	78
375	106	111	105
376	75	69	78
377	78	82	82
378	97	74	120
379	80	75	87
380	68	70	86

MEAN	83	80	89
SD	11.6	13.0	13.9
N	10	10	10

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Triglycerides

STUDY ID: 107
STUDY NO: 107
ABBR: TRY

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	61	51	98
352	62	56	76
353	54	71	123
354	119	103	122
355	69	125	164
356	72	63	96
357	70	80	111
358	54	61	58
359	29	38	42
360	82	48	139

MEAN	67	70	103
SD	23.1	26.7	37.1
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	112	146	180
372	142	110	119
373	74	109	107
374	64	95	93
375	114	135	232
376	117	228	277
377	80	140	103
378	48	65	100
379	74	113	121
380	40	94	67

MEAN	87	124	140
SD	33.2	44.0	67.7
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Blood Urea Nitrogen

STUDY ID: 107
STUDY NO: 107
ABBR: BUN

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	25.8	21.3	21.6
312	17.0	17.6	14.0
313	20.0	24.5	25.1
314	17.4	20.9	15.3
315	17.0	16.7	21.0
316	16.3	15.5	13.8
317	15.0	21.1	16.4
318	20.6	15.3	18.3
319	20.0	16.4	15.6
320	18.4	19.2	6.2

MEAN	18.8	18.9	16.7
SD	3.06	3.04	5.22
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	16.9	17.9	13.7
332	14.3	17.5	16.6
333	16.8	15.3	14.3
334	25.3	21.8	21.6
335	20.6	17.6	18.0
336	20.5	16.4	18.2
337	15.5	23.2	16.0
338	18.3	16.1	19.0
339	15.5	13.3	17.5
340	16.7	22.8	17.8

MEAN	18.0	18.2	17.3
SD	3.28	3.34	2.29
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Blood Urea Nitrogen

STUDY ID: 107
STUDY NO: 107
ABBR: BUN

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	22.2	18.4	18.6
352	14.5	12.4	19.3
353	17.6	17.8	17.9
354	18.3	17.9	17.1
355	22.9	20.8	24.2
356	19.3	15.4	16.4
357	21.0	23.5	20.5
358	18.4	21.8	17.7
359	15.4	17.1	17.9
360	18.8	18.1	18.9

MEAN	18.8	18.3	18.9
SD	2.69	3.17	2.21
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	25.6	18.3	26.5
372	15.6	19.9	15.5
373	17.1	14.7	19.7
374	13.8	15.6	15.2
375	15.6	18.3	17.7
376	25.6	23.1	21.0
377	14.3	15.2	12.9
378	16.3	15.6	16.2
379	21.6	18.2	16.1
380	12.6	18.2	14.6

MEAN	17.8	17.7	17.5
SD	4.76	2.57	3.95
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Creatinine

STUDY ID: 107
STUDY NO: 107
ABBR: CREA

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	0.53	0.55	0.58
312	0.51	0.60	0.57
313	0.64	0.78	0.73
314	0.50	0.53	0.55
315	0.57	0.65	0.65
316	0.61	0.65	0.70
317	0.62	0.59	0.75
318	0.62	0.64	0.70
319	0.49	0.54	0.52
320	0.66	0.64	0.60

MEAN	0.58	0.62	0.64
SD	0.063	0.074	0.082
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	0.55	0.65	0.62
332	0.54	0.69	0.63
333	0.54	0.75	0.63
334	0.59	0.57	0.70
335	0.55	0.65	0.61
336	0.65	0.69	0.68
337	0.60	0.71	0.71
338	0.52	0.59	0.62
339	0.71	0.56	0.62
340	0.68	0.65	0.60

MEAN	0.59	0.65	0.64
SD	0.066	0.062	0.039
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Creatinine

STUDY ID: 107
STUDY NO: 107
ABBR: CREA

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	0.58	0.56	0.56
352	0.59	0.62	0.74
353	0.46	0.54	0.56
354	0.57	0.60	0.60
355	0.62	0.57	0.62
356	0.60	0.60	0.77
357	0.58	0.63	0.63
358	0.59	0.63	0.64
359	0.53	0.58	0.60
360	0.57	0.74	0.72

MEAN	0.57	0.61	0.64
SD	0.045	0.056	0.074
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	0.59	0.63	0.66
372	0.47	0.60	0.65
373	0.51	0.55	0.64
374	0.64	0.55	0.80
375	0.59	0.68	0.56
376	0.55	0.61	0.72
377	0.61	0.62	0.63
378	0.50	0.62	0.56
379	0.51	0.61	0.64
380	0.54	0.57	0.60

MEAN	0.55	0.60	0.65
SD	0.055	0.039	0.072
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Sodium

STUDY ID: 107
STUDY NO: 107
ABBR: NA

SEX: FEMALE

UNITS: mmol/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	140	142	145
312	141	140	145
313	141	141	141
314	142	144	142
315	144	145	144
316	143	143	145
317	144	143	145
318	144	144	145
319	141	143	144
320	143	144	145

MEAN	142	143	144
SD	1.5	1.5	1.4
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	142	146	140
332	142	144	144
333	144	146	147
334	144	140	144
335	142	143	143
336	143	146	150
337	144	143	144
338	142	140	142
339	146	144	146
340	144	145	144

MEAN	143	144	144
SD	1.3	2.3	2.8
N	10	10	10

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Sodium

STUDY ID: 107
STUDY NO: 107
ABBR: NA

SEX: FEMALE

UNITS: mmol/L

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 3-F:1.5 mg base/kg/day

351	144	143	143
352	144	145	144
353	142	145	147
354	143	144	143
355	144	142	146
356	145	144	147
357	146	140	144
358	143	142	142
359	144	143	145
360	145	142	144

MEAN	144	143	145
SD	1.2	1.6	1.7
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	143	145	144
372	143	143	145
373	145	142	143
374	145	141	146
375	146	146	144
376	141	141	145
377	143	142	147
378	143	141	144
379	143	142	145
380	146	143	145

MEAN	144	143	145
SD	1.6	1.7	1.1
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Potassium

STUDY ID: 107
STUDY NO: 107
ABBR: K

SEX: FEMALE

UNITS: mmol/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	6.40	5.86	5.84
312	5.59	5.91	5.16
313	5.58	5.15	5.39
314	5.32	5.38	5.38
315	5.68	5.71	5.75
316	5.66	6.52	5.68
317	6.18	5.20	4.44
318	5.67	5.59	5.24
319	6.71	6.15	5.86
320	5.29	5.37	4.93

MEAN	5.81	5.68	5.37
SD	0.467	0.437	0.450
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	5.42	5.44	5.16
332	5.61	5.44	5.83
333	5.41	4.97	5.66
334	5.73	5.83	4.96
335	5.12	5.50	5.61
336	5.21	5.61	4.97
337	5.40	5.02	5.92
338	6.37	5.92	6.35
339	5.40	5.14	5.47
340	5.52	5.71	5.73

MEAN	5.52	5.46	5.57
SD	0.347	0.329	0.440
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Potassium

STUDY ID: 107
STUDY NO: 107
ABBR: K

SEX: FEMALE

UNITS: mmol/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	5.51	5.46	5.43
352	5.38	5.40	5.56
353	5.51	5.41	6.00
354	5.59	5.54	5.24
355	5.62	5.04	5.49
356	6.39	5.09	6.28
357	6.14	5.49	5.89
358	5.43	6.14	5.46
359	5.42	5.67	5.39
360	5.66	4.90	5.79

MEAN	5.67	5.41	5.65
SD	0.334	0.354	0.325
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	5.34	5.82	5.35
372	5.56	5.42	5.36
373	5.30	5.46	5.65
374	5.57	5.21	5.77
375	6.08	5.66	5.84
376	5.21	5.23	5.49
377	6.29	5.31	5.69
378	5.39	5.27	5.62
379	5.58	4.95	5.05
380	5.75	5.46	5.65

MEAN	5.61	5.38	5.55
SD	0.347	0.245	0.237
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Chloride

STUDY ID: 107
STUDY NO: 107
ABBR: CL

SEX: FEMALE

UNITS: mEq/L

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
GROUP: 1-F:0 mg base/kg/day			
311	124	116	112
312	114	114	118
313	110	117	119
314	118	122	118
315	113	110	119
316	123	119	117
317	126	111	115
318	121	112	109
319	118	118	115
320	116	112	115
MEAN	118	115	116
SD	5.2	3.9	3.2
N	10	10	10

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
GROUP: 2-F:0.5 mg base/kg/day			
331	116	119	121
332	113	113	118
333	118	120	113
334	117	117	114
335	124	111	119
336	112	113	121
337	123	118	120
338	119	115	119
339	125	109	110
340	125	121	113
MEAN	119	116	117
SD	4.8	4.0	3.9
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Chloride

STUDY ID: 107
STUDY NO: 107
ABBR: CL

SEX: FEMALE

UNITS: mEq/L

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	120	116	110
352	115	113	114
353	119	121	112
354	113	109	115
355	120	113	114
356	115	113	119
357	116	118	123
358	119	117	124
359	117	108	112
360	112	123	111
MEAN	117	115	115
SD	2.9	4.8	4.9
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	116	109	117
372	116	110	117
373	114	110	114
374	111	112	114
375	113	126	121
376	123	117	116
377	114	118	115
378	116	117	117
379	114	123	111
380	107	116	111
MEAN	114	116	115
SD	4.1	5.7	3.0
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Calcium

STUDY ID: 107
STUDY NO: 107
ABBR: CA

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	11.7	11.2	11.2
312	11.0	11.2	11.5
313	11.6	11.1	11.4
314	11.5	11.4	11.8
315	11.6	12.5	12.1
316	11.6	10.8	11.1
317	12.0	11.3	11.8
318	12.0	11.3	11.0
319	11.0	11.8	10.7
320	12.0	11.0	10.2

MEAN	11.6	11.4	11.3
SD	0.37	0.48	0.57
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	10.7	10.1	11.1
332	11.1	11.2	12.0
333	11.4	11.6	12.2
334	12.3	11.1	12.5
335	11.7	11.4	11.8
336	10.9	12.2	13.1
337	11.1	11.7	11.6
338	11.2	11.6	11.2
339	11.6	10.9	12.2
340	11.9	10.9	12.8

MEAN	11.4	11.3	12.1
SD	0.49	0.57	0.65
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Calcium

STUDY ID: 107
STUDY NO: 107
ABBR: CA

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	11.9	11.0	11.6
352	11.6	11.6	11.3
353	11.2	11.3	12.1
354	12.0	11.7	12.7
355	11.8	11.8	11.6
356	12.5	11.6	12.4
357	11.3	11.5	12.1
358	11.7	11.2	11.5
359	11.1	11.7	11.8
360	11.1	11.2	11.5

MEAN	11.6	11.5	11.9
SD	0.45	0.27	0.45
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	12.6	12.7	12.7
372	11.9	11.4	11.4
373	12.0	12.4	12.2
374	11.9	11.5	12.9
375	11.4	11.8	12.1
376	12.0	11.6	11.9
377	11.7	11.3	12.3
378	11.6	12.1	12.7
379	11.7	12.0	11.5
380	11.3	11.3	11.5

MEAN	11.8	11.8	12.1
SD	0.37	0.48	0.54
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Inorganic Phosphorus

STUDY ID: 107
STUDY NO: 107
ABBR: IP

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	8.9	8.4	6.8
312	9.0	8.2	6.6
313	8.3	9.1	8.6
314	7.4	6.6	5.7
315	6.5	6.3	8.4
316	9.3	7.4	6.2
317	10.6	7.5	8.3
318	7.3	8.4	7.7
319	9.5	8.5	6.7
320	8.6	6.3	6.1

MEAN	8.5	7.7	7.1
SD	1.21	1.00	1.05
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	9.8	9.7	7.8
332	6.9	5.8	7.1
333	8.7	10.3	7.1
334	10.3	8.7	7.0
335	8.2	7.4	7.2
336	8.7	7.7	6.6
337	8.5	8.4	9.5
338	8.9	7.6	8.7
339	9.4	6.3	7.6
340	11.3	7.9	8.2

MEAN	9.1	8.0	7.7
SD	1.21	1.38	0.89
N	10	10	10

LABCAT CC4.25

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Inorganic PhosphorusSTUDY ID: 107
STUDY NO: 107
ABBR: IP

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 3-F:1.5 mg base/kg/day

351	9.7	7.8	7.7
352	7.0	7.4	7.4
353	8.1	8.8	6.9
354	9.3	7.3	7.1
355	11.6	8.6	7.3
356	10.7	6.7	10.2
357	8.7	8.2	7.9
358	8.6	6.1	7.1
359	8.2	7.0	7.1
360	6.7	9.6	7.3

MEAN	8.9	7.8	7.6
SD	1.53	1.06	0.96
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	8.9	8.7	7.7
372	8.7	7.0	6.7
373	9.3	9.1	6.8
374	9.7	8.2	8.4
375	9.2	8.2	7.9
376	8.8	8.8	8.5
377	9.7	7.5	7.1
378	9.4	8.5	7.6
379	9.6	10.1	7.5
380	8.7	8.9	6.9

MEAN	9.2	8.5	7.5
SD	0.40	0.86	0.64
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Glucose

STUDY ID: 107
STUDY NO: 107
ABBR: GLU

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	159	125	111
312	144	176	188
313	143	161	141
314	144	117	162
315	137	116	147
316	157	134	138
317	229	130	257
318	165	136	136
319	138	122	130
320	143	136	155

MEAN	156	135	157
SD	27.3	19.3	40.8
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	154	198	163
332	150	137	123
333	161	191	154
334	242	163	149
335	169	129	142
336	158	132	222
337	125	197	163
338	174	151	146
339	228	143	140
340	181	145	190

MEAN	174	159	159
SD	35.6	27.1	28.3
N	10	10	10

LABCAT CC4.25

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Glucose

STUDY ID: 107
STUDY NO: 107
ABBR: GLU

SEX: FEMALE

UNITS: mg/dL

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 3-F:1.5 mg base/kg/day

351	150	140	137
352	149	138	131
353	148	126	132
354	139	143	129
355	208	138	139
356	204	140	158
357	157	158	150
358	131	157	163
359	132	122	132
360	128	206	146

MEAN	155	147	142
SD	28.7	23.7	12.0
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	125	110	127
372	164	142	132
373	156	123	139
374	148	139	135
375	134	143	169
376	149	106	111
377	188	128	126
378	124	117	142
379	143	160	121
380	132	117	120

MEAN	146	129	132
SD	19.6	17.1	16.0
N	10	10	10

LABCAT CC4.25

APPENDIX 7

Individual Hematology Data

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Erythrocytes

STUDY ID: 107
STUDY NO: 107
ABBR: RBC

SEX: MALE

UNITS: $10^6/\text{cmm}$

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	7.79	8.80	9.15
302	7.79	8.35	9.08
303	7.47	8.26	8.05
304	7.29	8.16	8.54
305	8.16	8.86	8.82
306	7.56	8.66	8.65
307	7.59	8.34	8.37
308	7.92	8.35	8.78
309	7.06	7.66	8.06
310	7.56	8.13	8.55

MEAN	7.62	8.36	8.61
SD	0.315	0.354	0.376
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	7.71	8.61	8.51
322	7.55	7.97	8.36
323	7.83	7.80	7.72
324	7.51	8.01	8.85
325	7.50	8.46	8.29
326	7.72	8.86	8.39
327	7.34	7.41	7.57
328	7.62	7.49	8.12
329	7.64	8.09	8.61
330	7.80	8.36	8.68

MEAN	7.62	8.11	8.31
SD	0.151	0.471	0.408
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Erythrocytes

STUDY ID: 107
STUDY NO: 107
ABBR: RBC

SEX: MALE

UNITS: $10^6/\text{cmm}$

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	6.42	8.07	7.71
342	7.19	7.49	6.76
343	6.61	7.33	7.89
344	6.58	7.52	7.78
345	7.04	7.92	7.89
346	6.93	7.63	7.99
347	6.72	7.80	7.56
348	6.83	8.04	7.69
349	6.95	7.82	8.13
350	6.75	7.44	7.48

MEAN	6.80	7.71	7.69
SD	0.233	0.261	0.380
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	7.95	9.97	8.63
363	--	--	--
364	7.05	10.69	9.02
365	7.23	7.69	8.05
366	--	--	--
367	8.92	9.70	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	7.79	9.51	8.57
SD	0.849	1.285	0.488
N	4	4	3

(--)-Data Unavailable

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Hemoglobin

STUDY ID: 107
STUDY NO: 107
ABBR: HGB

SEX: MALE

UNITS: g/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	15.8	15.7	16.1
302	16.8	16.8	16.6
303	15.7	16.6	15.7
304	15.2	15.7	15.8
305	16.8	17.0	16.8
306	16.7	17.4	17.0
307	16.0	15.7	15.2
308	15.9	15.2	16.2
309	14.6	14.7	14.6
310	16.0	16.0	15.7

MEAN	16.0	16.1	16.0
SD	0.71	0.85	0.73
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	15.6	16.3	15.4
322	15.8	15.9	15.8
323	16.2	15.5	15.0
324	15.8	16.1	16.5
325	16.2	17.4	15.9
326	16.2	17.7	17.2
327	15.1	15.1	14.6
328	15.7	15.1	15.9
329	15.5	15.6	15.5
330	17.0	17.7	17.1

MEAN	15.9	16.2	15.9
SD	0.52	1.02	0.84
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Hemoglobin

STUDY ID: 107
STUDY NO: 107
ABBR: HGB

SEX: MALE

UNITS: g/dL

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
GROUP: 3-M:1.5 mg base/kg/day			
341	14.1	16.3	14.9
342	15.8	15.5	13.1
343	14.1	15.1	15.2
344	14.5	14.9	15.0
345	14.6	15.0	14.8
346	15.4	15.5	15.2
347	15.0	15.9	14.7
348	15.1	16.3	15.2
349	14.5	14.8	15.0
350	14.9	14.9	15.0
MEAN	14.8	15.4	14.8
SD	0.55	0.58	0.62
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day			
361	--	--	--
362	15.1	18.5	16.2
363	--	--	--
364	14.6	18.8	17.6
365	15.1	14.9	15.0
366	--	--	--
367	18.1	19.5	--
368	--	--	--
369	--	--	--
370	--	--	--
MEAN	15.7	17.9	16.3
SD	1.60	2.06	1.30
N	4	4	3

(--)-Data Unavailable

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Hematocrit

STUDY ID: 107
STUDY NO: 107
ABBR: HCT

SEX: MALE

UNITS: %

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	43.7	45.7	46.2
302	47.0	47.3	48.0
303	44.3	46.4	44.2
304	42.4	44.6	45.2
305	48.2	49.2	48.2
306	45.6	48.8	47.2
307	43.3	44.5	43.0
308	44.3	43.6	44.1
309	41.4	41.1	41.7
310	43.5	43.7	44.2

MEAN	44.4	45.5	45.2
SD	2.06	2.51	2.16
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	43.1	45.6	43.5
322	44.8	45.8	45.7
323	45.6	44.4	41.8
324	44.6	46.4	47.7
325	45.3	49.7	45.3
326	47.0	51.8	48.4
327	42.4	41.5	41.0
328	44.3	42.5	45.3
329	43.2	43.8	43.7
330	47.6	50.0	49.5

MEAN	44.8	46.2	45.2
SD	1.67	3.39	2.78
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Hematocrit

STUDY ID: 107
STUDY NO: 107
ABBR: HCT

SEX: MALE

UNITS: %

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	40.4	46.6	42.7
342	45.4	44.0	38.0
343	41.5	44.6	45.2
344	41.3	43.4	43.1
345	42.2	44.1	42.2
346	43.4	44.8	44.3
347	41.9	45.9	43.0
348	43.0	47.2	43.8
349	41.6	44.0	44.0
350	42.9	43.7	43.5

MEAN	42.4	44.8	43.0
SD	1.40	1.30	1.95
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	43.9	54.1	46.9
363	--	--	--
364	41.2	55.8	50.8
365	44.3	43.5	44.8
366	--	--	--
367	50.8	55.3	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	45.1	52.2	47.5
SD	4.07	5.83	3.04
N	4	4	3

(--)-Data Unavailable

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Mean Corpuscular Volume

STUDY ID: 107
STUDY NO: 107
ABBR: MCV

SEX: MALE

UNITS: fL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	56.1	51.9	50.5
302	60.3	56.6	52.9
303	59.3	56.2	54.9
304	58.2	54.7	52.9
305	59.1	55.5	54.6
306	60.3	56.4	54.6
307	57.0	53.4	51.4
308	55.9	52.2	50.2
309	58.6	53.7	51.7
310	57.5	53.8	51.7

MEAN	58.2	54.4	52.5
SD	1.59	1.71	1.72
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	55.9	53.0	51.1
322	59.3	57.5	54.7
323	58.2	56.9	54.1
324	59.4	57.9	53.9
325	60.4	58.7	54.6
326	60.9	58.5	57.7
327	57.8	56.0	54.2
328	58.1	56.7	55.8
329	56.5	54.1	50.8
330	61.0	59.8	57.0

MEAN	58.8	56.9	54.4
SD	1.76	2.09	2.21
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Mean Corpuscular Volume

STUDY ID: 107
STUDY NO: 107
ABBR: MCV

SEX: MALE

UNITS: fL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	62.9	57.7	55.4
342	63.1	58.7	56.2
343	62.8	60.8	57.3
344	62.8	57.7	55.4
345	59.9	55.7	53.5
346	62.6	58.7	55.4
347	62.4	58.8	56.9
348	63.0	58.7	57.0
349	59.9	56.3	54.1
350	63.6	58.7	58.2

MEAN	62.3	58.2	55.9
SD	1.30	1.43	1.46
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	55.2	54.3	54.3
363	--	--	--
364	58.4	52.2	56.3
365	61.3	56.6	55.7
366	--	--	--
367	57.0	57.0	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	58.0	55.0	55.4
SD	2.57	2.23	1.03
N	4	4	3

(--)-Data Unavailable

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Mean Corpuscular Hemoglobin

STUDY ID: 107

SEX: MALE

STUDY NO: 107

ABBR: MCH

UNITS: pg

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 1-M:0 mg base/kg/day

301	20.3	17.8	17.6
302	21.6	20.1	18.3
303	21.0	20.1	19.5
304	20.9	19.2	18.5
305	20.6	19.2	19.0
306	22.1	20.1	19.7
307	21.1	18.8	18.2
308	20.1	18.2	18.5
309	20.7	19.2	18.1
310	21.2	19.7	18.4

MEAN	21.0	19.2	18.6
SD	0.59	0.80	0.64
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	20.2	18.9	18.1
322	20.9	19.9	18.9
323	20.7	19.9	19.4
324	21.0	20.1	18.6
325	21.6	20.6	19.2
326	21.0	20.0	20.5
327	20.6	20.4	19.3
328	20.6	20.2	19.6
329	20.3	19.3	18.0
330	21.8	21.2	19.7

MEAN	20.9	20.1	19.1
SD	0.51	0.64	0.76
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Mean Corpuscular Hemoglobin

STUDY ID: 107
STUDY NO: 107
ABBR: MCH

SEX: MALE

UNITS: pg

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
-----------	--------	--------	---------

GROUP: 3-M:1.5 mg base/kg/day

341	22.0	20.2	19.3
342	22.0	20.7	19.4
343	21.3	20.6	19.3
344	22.0	19.8	19.3
345	20.7	18.9	18.8
346	22.2	20.3	19.0
347	22.3	20.4	19.4
348	22.1	20.3	19.8
349	20.9	18.9	18.5
350	22.1	20.0	20.1

MEAN	21.8	20.0	19.3
SD	0.57	0.64	0.46
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	19.0	18.6	18.8
363	--	--	--
364	20.7	17.6	19.5
365	20.9	19.4	18.6
366	--	--	--
367	20.3	20.1	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	20.2	18.9	19.0
SD	0.85	1.08	0.47
N	4	4	3

(--)-Data Unavailable

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Mean Corpus. Hemo. Conc.

STUDY ID: 107
STUDY NO: 107
ABBR: MCHC

SEX: MALE

UNITS: g/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	36.2	34.4	34.8
302	35.7	35.5	34.6
303	35.4	35.8	35.5
304	35.8	35.2	35.0
305	34.9	34.6	34.9
306	36.6	35.7	36.0
307	37.0	35.3	35.3
308	35.9	34.9	36.7
309	35.3	35.8	35.0
310	36.8	36.6	35.5

MEAN	36.0	35.4	35.3
SD	0.69	0.65	0.63
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	36.2	35.7	35.4
322	35.3	34.7	34.6
323	35.5	34.9	35.9
324	35.4	34.7	34.6
325	35.8	35.0	35.1
326	34.5	34.2	35.5
327	35.6	36.4	35.6
328	35.4	35.5	35.1
329	35.9	35.6	35.5
330	35.7	35.4	34.5

MEAN	35.5	35.2	35.2
SD	0.45	0.63	0.48
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Mean Corpus. Hemo. Conc.

STUDY ID: 107
STUDY NO: 107
ABBR: MCHC

SEX: MALE

UNITS: g/dL

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 3-M:1.5 mg base/kg/day

341	34.9	35.0	34.9
342	34.8	35.2	34.5
343	34.0	33.9	33.6
344	35.1	34.3	34.8
345	34.6	34.0	35.1
346	35.5	34.6	34.3
347	35.8	34.6	34.2
348	35.1	34.5	34.7
349	34.9	33.6	34.1
350	34.7	34.1	34.5

MEAN	34.9	34.4	34.5
SD	0.49	0.50	0.44
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	34.4	34.2	34.5
363	--	--	--
364	35.4	33.7	34.6
365	34.1	34.3	33.5
366	--	--	--
367	35.6	35.3	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	34.9	34.4	34.2
SD	0.74	0.67	0.61
N	4	4	3

(--)-Data Unavailable

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Reticulocyte Count

STUDY ID: 107
ABBR: RETICS

SEX: MALE
UNITS: %RBCs

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
GROUP: 1-M:0 mg base/kg/day			
301	1.6	0.4	0.2
302	0.3	1.4	0.6
303	1.3	0.6	0.3
304	0.7	0.6	0.8
305	0.2	0.5	0.1
306	0.2	1.6	1.2
307	0.2	0.3	1.7
308	0.8	0.3	0.1
309	0.7	0.5	0.2
310	0.4	0.4	0.8
MEAN	0.6	0.7	0.6
SD	0.49	0.46	0.53
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day			
321	0.7	0.4	1.3
322	2.4	0.7	1.1
323	1.1	1.0	0.7
324	0.3	0.6	0.2
325	0.4	1.7	0.7
326	2.0	0.4	0.3
327	1.6	0.3	0.6
328	1.4	0.3	1.4
329	0.4	0.9	0.1
330	1.2	0.7	1.2
MEAN	1.2	0.7	0.8
SD	0.72	0.43	0.47
N	10	10	10

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THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Reticulocyte Count

STUDY ID: 107
ABBR: RETICS

SEX: MALE
UNITS: %RBCs

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 3-M:1.5 mg base/kg/day

341	3.8	1.2	1.3
342	3.2	0.4	1.4
343	5.1	1.4	1.3
344	1.4	0.6	0.8
345	2.8	1.1	0.4
346	1.1	0.9	0.4
347	1.1	1.3	1.4
348	1.8	1.4	1.6
349	1.0	0.7	0.4
350	2.3	1.9	0.6

MEAN	2.4	1.1	1.0
SD	1.36	0.45	0.49
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	1.0	2.4	0.8
363	--	--	--
364	1.5	0.3	1.3
365	4.8	2.0	1.6
366	--	--	--
367	1.2	2.6	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	2.1	1.8	1.2
SD	1.80	1.05	0.40
N	4	4	3

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Nucleated Red Cells

STUDY ID: 107
STUDY NO: 107
ABBR: NRBC

SEX: MALE

UNITS: COUNT

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 1-M:0 mg base/kg/day

301	0	0	0
302	0	0	0
303	0	0	0
304	0	0	0
305	0	0	0
306	0	0	0
307	0	0	0
308	0	0	0
309	0	0	0
310	0	0	0

MEAN	0	0	0
SD	0.0	0.0	0.0
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	0	0	0
322	0	0	0
323	0	0	0
324	0	0	0
325	0	0	0
326	0	0	0
327	0	0	0
328	0	0	0
329	0	0	0
330	0	0	0

MEAN	0	0	0
SD	0.0	0.0	0.0
N	10	10	10

WBC corrected for NRBC = or > 10

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THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Nucleated Red Cells

STUDY ID: 107
STUDY NO: 107
ABBR: NRBC

SEX: MALE

UNITS: COUNT

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 3-M:1.5 mg base/kg/day

341	0	0	0
342	0	0	0
343	0	0	0
344	0	0	0
345	0	0	0
346	0	0	0
347	0	0	0
348	0	0	0
349	0	0	0
350	0	0	0

MEAN	0	0	0
SD	0.0	0.0	0.0
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	0	0	0
363	--	--	--
364	0	0	0
365	0	0	0
366	--	--	--
367	0	0	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	0	0	0
SD	0.0	0.0	0.0
N	4	4	3

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Heinz Bodies

STUDY ID: 107
STUDY NO: 107
ABBR: HB

SEX: MALE

UNITS: %

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	0.0	0.0	0.1
302	0.0	0.0	0.0
303	0.0	0.0	0.0
304	0.0	0.0	0.3
305	0.0	0.0	0.0
306	0.0	0.2	0.4
307	0.0	0.0	0.3
308	0.0	0.0	0.0
309	0.0	0.0	0.3
310	0.0	0.0	0.0

MEAN	0.0	0.0	0.1
SD	0.00	0.06	0.16
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	0.0	0.3	0.0
322	0.0	0.0	0.2
323	0.0	0.0	0.0
324	0.0	0.0	0.1
325	0.0	0.0	0.2
326	0.0	0.0	0.0
327	0.0	0.0	0.0
328	0.0	0.0	0.2
329	0.0	0.0	0.0
330	0.0	0.0	0.2

MEAN	0.0	0.0	0.1
SD	0.00	0.09	0.10
N	10	10	10

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THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Heinz Bodies

STUDY ID: 107
STUDY NO: 107
ABBR: HB

SEX: MALE

UNITS: %

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	0.7	0.2	1.1
342	0.1	0.2	0.2
343	0.0	0.6	0.4
344	0.6	0.5	0.0
345	0.0	0.5	0.0
346	0.4	0.2	0.3
347	0.3	0.2	0.6
348	0.3	0.1	0.1
349	0.5	0.4	0.1
350	0.4	0.9	0.0

MEAN	0.3	0.4	0.3
SD	0.24	0.25	0.35
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	0.4	0.2	0.3
363	--	--	--
364	0.3	0.0	0.4
365	0.1	0.5	1.1
366	--	--	--
367	0.2	0.0	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	0.3	0.2	0.6
SD	0.13	0.24	0.44
N	4	4	3

(--)-Data Unavailable

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: % Methemoglobin

STUDY ID: 107
STUDY NO: 107
ABBR: %METHGB

SEX: MALE

UNITS: %

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-M:0 mg base/kg/day

301	0.9	0.8	0.7
302	0.3	1.3	0.6
303	0.8	0.8	0.7
304	0.8	0.9	0.9
305	0.5	0.5	0.6
306	1.0	1.3	1.3
307	0.7	0.7	0.9
308	0.7	0.6	0.8
309	0.8	1.0	0.8
310	0.7	1.0	1.0

MEAN	0.7	0.9	0.8
SD	0.20	0.27	0.21
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	2.1	1.6	2.2
322	1.9	2.2	2.2
323	1.8	1.7	2.3
324	1.3	1.1	1.4
325	2.0	2.2	2.2
326	1.9	2.2	1.6
327	1.4	1.9	1.6
328	1.9	1.8	1.4
329	1.3	1.6	1.6
330	1.4	1.7	1.3

MEAN	1.7	1.8	1.8
SD	0.31	0.35	0.40
N	10	10	10

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THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: % Methemoglobin

STUDY ID: 107
STUDY NO: 107
ABBR: %METHGB

SEX: MALE

UNITS: %

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 3-M:1.5 mg base/kg/day

341	4.1	5.4	4.9
342	5.5	5.8	5.4
343	5.1	5.3	6.2
344	4.6	4.6	5.3
345	5.2	6.5	7.6
346	3.2	3.6	4.0
347	6.1	7.4	6.6
348	5.4	7.6	7.3
349	2.6	3.5	4.7
350	5.2	6.2	6.1

MEAN	4.7	5.6	5.8
SD	1.09	1.41	1.16
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	10.3	7.1	8.1
363	--	--	--
364	6.9	4.2	5.8
365	6.6	10.5	11.9
366	--	--	--
367	3.7	5.2	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	6.9	6.8	8.6
SD	2.70	2.77	3.08
N	4	4	3

(--)-Data Unavailable

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Platelets

STUDY ID: 107
STUDY NO: 107
ABBR: PLT

SEX: MALE

UNITS: $10^3/\text{ccm}$

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 1-M:0 mg base/kg/day

301	1080	1085	1163
302	1133	925	934
303	1140	1175	1063
304	986	1007	930
305	1099	1029	1018
306	1004	1064	1041
307	1286	1254	1193
308	1113	1188	1155
309	1123	1107	1078
310	1055	1087	1087

MEAN	1102	1092	1066
SD	83.4	95.8	90.0
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	1124	1080	1056
322	1111	1001	988
323	1061	902	953
324	808	913	851
325	1021	804	884
326	1055	1068	975
327	1101	1007	1031
328	1192	1006	1063
329	976	874	853
330	917	887	923

MEAN	1037	954	958
SD	112.0	90.9	79.1
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Platelets

STUDY ID: 107
STUDY NO: 107
ABBR: PLT

SEX: MALE

UNITS: $10^3/\text{ccm}$

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-M:1.5 mg base/kg/day

341	1171	992	953
342	896	843	669
343	1037	1040	731
344	998	996	993
345	1087	1050	1084
346	1076	1028	992
347	982	930	919
348	973	784	829
349	1237	1169	1133
350	1095	1003	1012

MEAN	1055	984	932
SD	100.3	109.0	148.3
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	1224	476	1014
363	--	--	--
364	724	687	815
365	714	867	663
366	--	--	--
367	974	529	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	909	640	831
SD	242.0	176.0	176.0
N	4	4	3

(--)-Data Unavailable

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Leukocytes

STUDY ID: 107
STUDY NO: 107
ABBR: WBC

SEX: MALE

UNITS: $10^3/\text{ccm}$

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 1-M:0 mg base/kg/day

301	16.0	15.3	14.5
302	20.1	18.1	17.0
303	13.9	13.5	10.7
304	12.7	16.6	13.8
305	25.9	24.2	19.5
306	19.0	17.2	16.5
307	25.7	21.1	18.2
308	17.4	15.5	16.1
309	13.9	16.5	14.9
310	20.1	18.5	16.7

MEAN	18.5	17.7	15.8
SD	4.66	3.09	2.47
N	10	10	10

GROUP: 2-M:0.5 mg base/kg/day

321	22.5	17.1	13.8
322	18.7	15.9	17.0
323	22.2	20.1	18.4
324	17.0	15.9	16.1
325	21.3	17.6	16.2
326	23.2	23.0	21.7
327	15.8	14.3	17.9
328	14.5	10.9	14.6
329	25.3	23.2	21.3
330	22.2	18.3	16.7

MEAN	20.3	17.6	17.4
SD	3.56	3.79	2.57
N	10	10	10

WBC corrected for NRBC = or > 10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Leukocytes

STUDY ID: 107
STUDY NO: 107
ABBR: WBC

SEX: MALE

UNITS: $10^3/\text{ccm}$

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 3-M:1.5 mg base/kg/day

341	25.9	28.5	29.8
342	23.1	24.4	13.4
343	24.7	23.5	25.4
344	26.6	23.2	19.5
345	25.3	21.5	22.6
346	26.0	23.7	28.3
347	20.8	21.4	18.4
348	24.5	27.6	24.5
349	23.8	20.9	17.8
350	27.1	31.9	28.4

MEAN	24.8	24.7	22.8
SD	1.87	3.57	5.42
N	10	10	10

GROUP: 4-M:4.5 mg base/kg/day

361	--	--	--
362	22.5	12.7	31.3
363	--	--	--
364	31.2	33.8	37.0
365	26.7	28.5	22.0
366	--	--	--
367	35.4	27.1	--
368	--	--	--
369	--	--	--
370	--	--	--

MEAN	29.0	25.5	30.1
SD	5.58	9.02	7.57
N	4	4	3

(--)-Data Unavailable

WBC corrected for NRBC = or > 10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

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WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 1-M : 0 mg base/kg/day

SEX: MALE

ANIMAL ID

WEEK 5

WEEK 9

WEEK 13

REL

ABS

REL

ABS

REL

ABS

301	Nucleated Red Cells	0		0		0	
	M. Neutrophils	19	3.0	16	2.4	16	2.3
	I. Neutrophils	1	0.2	0	0.0	4	0.6
	Lymphocytes	71	11.4	76	11.6	74	10.7
	Monocytes	8	1.3	6	0.9	5	0.7
	Eosinophils	1	0.2	2	0.3	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		16.0		15.3		14.5
302	Nucleated Red Cells	0		0		0	
	M. Neutrophils	16	3.2	21	3.8	18	3.1
	I. Neutrophils	1	0.2	0	0.0	2	0.3
	Lymphocytes	80	16.1	75	13.6	74	12.6
	Monocytes	1	0.2	1	0.2	3	0.5
	Eosinophils	2	0.4	3	0.5	2	0.3
	Basophils	0	0.0	0	0.0	1	0.2
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		20.1		18.1		17.0
303	Nucleated Red Cells	0		0		0	
	M. Neutrophils	9	1.3	15	2.0	10	1.1
	I. Neutrophils	1	0.1	0	0.0	2	0.2
	Lymphocytes	86	12.0	81	10.9	82	8.8
	Monocytes	4	0.6	4	0.5	5	0.5
	Eosinophils	0	0.0	0	0.0	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		13.9		13.5		10.7
304	Nucleated Red Cells	0		0		0	
	M. Neutrophils	13	1.7	4	0.7	8	1.1
	I. Neutrophils	0	0.0	2	0.3	2	0.3
	Lymphocytes	81	10.3	88	14.6	79	10.9
	Monocytes	2	0.3	5	0.8	7	1.0
	Eosinophils	4	0.5	1	0.2	4	0.6
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		12.7		16.6		13.8

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 107
STUDY NO: 107

GROUP: 1-M : 0 mg base/kg/day

SEX: MALE

ANIMAL ID		WEEK 5		WEEK 9		WEEK 13	
		REL	ABS	REL	ABS	REL	ABS
305	Nucleated Red Cells	0		0		0	
	M. Neutrophils	19	4.9	19	4.6	20	3.9
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	77	19.9	77	18.6	77	15.0
	Monocytes	4	1.0	4	1.0	3	0.6
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		25.9		24.2		19.5
306	Nucleated Red Cells	0		0		0	
	M. Neutrophils	15	2.9	10	1.7	13	2.1
	I. Neutrophils	0	0.0	4	0.7	1	0.2
	Lymphocytes	79	15.0	86	14.8	82	13.5
	Monocytes	4	0.8	0	0.0	4	0.7
	Eosinophils	2	0.4	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		19.0		17.2		16.5
307	Nucleated Red Cells	0		0		0	
	M. Neutrophils	5	1.3	6	1.3	7	1.3
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	91	23.4	89	18.8	89	16.2
	Monocytes	4	1.0	4	0.8	4	0.7
	Eosinophils	0	0.0	1	0.2	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		25.7		21.1		18.2
308	Nucleated Red Cells	0		0		0	
	M. Neutrophils	18	3.1	27	4.2	19	3.1
	I. Neutrophils	1	0.2	0	0.0	4	0.6
	Lymphocytes	76	13.2	69	10.7	71	11.4
	Monocytes	5	0.9	4	0.6	3	0.5
	Eosinophils	0	0.0	0	0.0	3	0.5
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		17.4		15.5		16.1

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 107
STUDY NO: 107

GROUP: 1-M : 0 mg base/kg/day

SEX: MALE

ANIMAL ID

WEEK 5
REL ABS

WEEK 9
REL ABS

WEEK 13
REL ABS

309	Nucleated Red Cells	0		0		0	
	M. Neutrophils	19	2.6	15	2.5	13	1.9
	I. Neutrophils	1	0.1	1	0.2	2	0.3
	Lymphocytes	79	11.0	82	13.5	81	12.1
	Monocytes	1	0.1	1	0.2	3	0.4
	Eosinophils	0	0.0	1	0.2	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		13.9		16.5		14.9
310	Nucleated Red Cells	0		0		0	
	M. Neutrophils	10	2.0	12	2.2	4	0.7
	I. Neutrophils	0	0.0	0	0.0	1	0.2
	Lymphocytes	88	17.7	85	15.7	94	15.7
	Monocytes	2	0.4	2	0.4	1	0.2
	Eosinophils	0	0.0	1	0.2	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		20.1		18.5		16.7

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 2-M : 0.5 mg base/kg/day

SEX: MALE

ANIMAL ID

WEEK 5
REL ABS

WEEK 9
REL ABS

WEEK 13
REL ABS

321	Nucleated Red Cells	0		0		0	
	M. Neutrophils	17	3.8	17	2.9	16	2.2
	I. Neutrophils	0	0.0	0	0.0	2	0.3
	Lymphocytes	80	18.0	82	14.0	82	11.3
	Monocytes	2	0.5	1	0.2	0	0.0
	Eosinophils	1	0.2	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		22.5		17.1		13.8
322	Nucleated Red Cells	0		0		0	
	M. Neutrophils	16	3.0	11	1.7	16	2.7
	I. Neutrophils	0	0.0	1	0.2	4	0.7
	Lymphocytes	81	15.1	85	13.5	76	12.9
	Monocytes	3	0.6	2	0.3	3	0.5
	Eosinophils	0	0.0	1	0.2	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		18.7		15.9		17.0
323	Nucleated Red Cells	0		0		0	
	M. Neutrophils	18	4.0	12	2.4	23	4.2
	I. Neutrophils	0	0.0	1	0.2	0	0.0
	Lymphocytes	77	17.1	82	16.5	76	14.0
	Monocytes	5	1.1	5	1.0	1	0.2
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		22.2		20.1		18.4
324	Nucleated Red Cells	0		0		0	
	M. Neutrophils	14	2.4	9	1.4	16	2.6
	I. Neutrophils	1	0.2	3	0.5	6	1.0
	Lymphocytes	79	13.4	81	12.9	78	12.6
	Monocytes	6	1.0	6	1.0	0	0.0
	Eosinophils	0	0.0	1	0.2	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		17.0		15.9		16.1

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 2-M : 0.5 mg base/kg/day

SEX: MALE

ANIMAL ID		WEEK 5		WEEK 9		WEEK 13	
		REL	ABS	REL	ABS	REL	ABS
325	Nucleated Red Cells	0		0		0	
	M. Neutrophils	16	3.4	8	1.4	7	1.1
	I. Neutrophils	0	0.0	2	0.4	7	1.1
	Lymphocytes	78	16.6	82	14.4	83	13.4
	Monocytes	4	0.9	7	1.2	1	0.2
	Eosinophils	1	0.2	1	0.2	1	0.2
	Basophils	1	0.2	0	0.0	1	0.2
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		21.3		17.6		16.2
326	Nucleated Red Cells	0		0		0	
	M. Neutrophils	14	3.2	11	2.5	25	5.4
	I. Neutrophils	0	0.0	1	0.2	2	0.4
	Lymphocytes	83	19.3	83	19.1	66	14.3
	Monocytes	3	0.7	5	1.2	6	1.3
	Eosinophils	0	0.0	0	0.0	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		23.2		23.0		21.7
327	Nucleated Red Cells	0		0		0	
	M. Neutrophils	13	2.1	7	1.0	12	2.1
	I. Neutrophils	1	0.2	0	0.0	5	0.9
	Lymphocytes	84	13.3	91	13.0	71	12.7
	Monocytes	1	0.2	1	0.1	12	2.1
	Eosinophils	1	0.2	1	0.1	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		15.8		14.3		17.9
328	Nucleated Red Cells	0		0		0	
	M. Neutrophils	17	2.5	7	0.8	7	1.0
	I. Neutrophils	2	0.3	0	0.0	2	0.3
	Lymphocytes	77	11.2	93	10.1	87	12.7
	Monocytes	2	0.3	0	0.0	4	0.6
	Eosinophils	2	0.3	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		14.5		10.9		14.6

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 107
STUDY NO: 107

GROUP: 2-M : 0.5 mg base/kg/day

SEX: MALE

ANIMAL ID

WEEK 5

WEEK 9

WEEK 13

REL

ABS

REL

ABS

REL

ABS

329

Nucleated Red Cells

0

0

0

M. Neutrophils

14

3.5

16

3.7

11

2.3

I. Neutrophils

2

0.5

3

0.7

5

1.1

Lymphocytes

76

19.2

76

17.6

76

16.2

Monocytes

8

2.0

5

1.2

8

1.7

Eosinophils

0

0.0

0

0.0

0

0.0

Basophils

0

0.0

0

0.0

0

0.0

Atypical Lymphocytes

0

0.0

0

0.0

0

0.0

WBC

25.3

23.2

21.3

330

Nucleated Red Cells

0

0

0

M. Neutrophils

19

4.2

11

2.0

11

1.8

I. Neutrophils

4

0.9

2

0.4

3

0.5

Lymphocytes

74

16.4

80

14.6

83

13.9

Monocytes

3

0.7

6

1.1

3

0.5

Eosinophils

0

0.0

1

0.2

0

0.0

Basophils

0

0.0

0

0.0

0

0.0

Atypical Lymphocytes

0

0.0

0

0.0

0

0.0

WBC

22.2

18.3

16.7

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 3-M : 1.5 mg base/kg/day

SEX: MALE

ANIMAL ID		WEEK 5		WEEK 9		WEEK 13	
		REL	ABS	REL	ABS	REL	ABS
341	Nucleated Red Cells	0		0		0	
	M. Neutrophils	17	4.4	15	4.3	21	6.3
	I. Neutrophils	1	0.3	3	0.9	0	0.0
	Lymphocytes	75	19.4	82	23.4	75	22.4
	Monocytes	6	1.6	0	0.0	4	1.2
	Eosinophils	1	0.3	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		25.9		28.5		29.8
342	Nucleated Red Cells	0		0		0	
	M. Neutrophils	18	4.2	15	3.7	25	3.4
	I. Neutrophils	3	0.7	1	0.2	6	0.8
	Lymphocytes	78	18.0	83	20.3	58	7.8
	Monocytes	1	0.2	1	0.2	7	0.9
	Eosinophils	0	0.0	0	0.0	4	0.5
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		23.1		24.4		13.4
343	Nucleated Red Cells	0		0		0	
	M. Neutrophils	13	3.2	16	3.8	12	3.0
	I. Neutrophils	2	0.5	0	0.0	7	1.8
	Lymphocytes	82	20.3	77	18.1	81	20.6
	Monocytes	3	0.7	7	1.6	0	0.0
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		24.7		23.5		25.4
344	Nucleated Red Cells	0		0		0	
	M. Neutrophils	22	5.9	24	5.6	24	4.7
	I. Neutrophils	1	0.3	0	0.0	4	0.8
	Lymphocytes	69	18.4	70	16.2	66	12.9
	Monocytes	7	1.9	5	1.2	6	1.2
	Eosinophils	1	0.3	1	0.2	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		26.6		23.2		19.5

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 3-M : 1.5 mg base/kg/day

SEX: MALE

ANIMAL ID		WEEK 5		WEEK 9		WEEK 13	
		REL	ABS	REL	ABS	REL	ABS
345	Nucleated Red Cells	0		0		0	
	M. Neutrophils	24	6.1	15	3.2	23	5.2
	I. Neutrophils	2	0.5	5	1.1	1	0.2
	Lymphocytes	72	18.2	79	17.0	69	15.6
	Monocytes	2	0.5	1	0.2	5	1.1
	Eosinophils	0	0.0	0	0.0	2	0.5
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		25.3		21.5		22.6
346	Nucleated Red Cells	0		0		0	
	M. Neutrophils	17	4.4	25	5.9	14	4.0
	I. Neutrophils	1	0.3	1	0.2	8	2.3
	Lymphocytes	79	20.5	70	16.6	75	21.2
	Monocytes	3	0.8	3	0.7	0	0.0
	Eosinophils	0	0.0	1	0.2	3	0.8
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		26.0		23.7		28.3
347	Nucleated Red Cells	0		0		0	
	M. Neutrophils	8	1.7	7	1.5	9	1.7
	I. Neutrophils	2	0.4	2	0.4	3	0.6
	Lymphocytes	82	17.1	87	18.6	85	15.6
	Monocytes	7	1.5	3	0.6	2	0.4
	Eosinophils	1	0.2	1	0.2	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		20.8		21.4		18.4
348	Nucleated Red Cells	0		0		0	
	M. Neutrophils	17	4.2	13	3.6	20	4.9
	I. Neutrophils	6	1.5	3	0.8	5	1.2
	Lymphocytes	75	18.4	83	22.9	65	15.9
	Monocytes	2	0.5	1	0.3	10	2.5
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		24.5		27.6		24.5

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 107
STUDY NO: 107

GROUP: 3-M : 1.5 mg base/kg/day

SEX: MALE

ANIMAL ID		WEEK 5		WEEK 9		WEEK 13	
		REL	ABS	REL	ABS	REL	ABS
349	Nucleated Red Cells	0		0		0	
	M. Neutrophils	33	7.9	23	4.8	19	3.4
	I. Neutrophils	2	0.5	3	0.6	3	0.5
	Lymphocytes	57	13.6	67	14.0	75	13.4
	Monocytes	7	1.7	7	1.5	1	0.2
	Eosinophils	1	0.2	0	0.0	2	0.4
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		23.8		20.9		17.8
350	Nucleated Red Cells	0		0		0	
	M. Neutrophils	13	3.5	7	2.2	9	2.6
	I. Neutrophils	4	1.1	2	0.6	2	0.6
	Lymphocytes	80	21.7	82	26.2	81	23.0
	Monocytes	1	0.3	8	2.6	5	1.4
	Eosinophils	2	0.5	1	0.3	3	0.9
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		27.1		31.9		28.4

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 4-M : 4.5 mg base/kg/day

SEX: MALE

ANIMAL ID

WEEK 5
REL ABS

WEEK 9
REL ABS

WEEK 13
REL ABS

361	Nucleated Red Cells	--	--	--	--	--	--
	M. Neutrophils	--	--	--	--	--	--
	I. Neutrophils	--	--	--	--	--	--
	Lymphocytes	--	--	--	--	--	--
	Monocytes	--	--	--	--	--	--
	Eosinophils	--	--	--	--	--	--
	Basophils	--	--	--	--	--	--
	Atypical Lymphocytes	--	--	--	--	--	--
	WBC	--	--	--	--	--	--
362	Nucleated Red Cells	0		0		0	
	M. Neutrophils	26	5.9	16	2.0	32	10.0
	I. Neutrophils	4	0.9	2	0.3	2	0.6
	Lymphocytes	64	14.4	61	7.7	59	18.5
	Monocytes	6	1.4	21	2.7	6	1.9
	Eosinophils	0	0.0	0	0.0	1	0.3
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		22.5		12.7		31.3
363	Nucleated Red Cells	--	--	--	--	--	--
	M. Neutrophils	--	--	--	--	--	--
	I. Neutrophils	--	--	--	--	--	--
	Lymphocytes	--	--	--	--	--	--
	Monocytes	--	--	--	--	--	--
	Eosinophils	--	--	--	--	--	--
	Basophils	--	--	--	--	--	--
	Atypical Lymphocytes	--	--	--	--	--	--
	WBC	--	--	--	--	--	--
364	Nucleated Red Cells	0		0		0	
	M. Neutrophils	22	6.9	24	8.1	22	8.1
	I. Neutrophils	2	0.6	2	0.7	2	0.7
	Lymphocytes	71	22.2	64	21.6	69	25.5
	Monocytes	4	1.2	8	2.7	7	2.6
	Eosinophils	1	0.3	2	0.7	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		31.2		33.8		37.0

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 4-M : 4.5 mg base/kg/day

SEX: MALE

ANIMAL ID

WEEK 5

WEEK 9

WEEK 13

REL

ABS

REL

ABS

REL

ABS

365

Nucleated Red Cells

0

0

0

M. Neutrophils

13

3.5

15

4.3

20

4.4

I. Neutrophils

1

0.3

0

0.0

2

0.4

Lymphocytes

78

20.8

66

18.8

73

16.1

Monocytes

7

1.9

17

4.8

4

0.9

Eosinophils

0

0.0

2

0.6

1

0.2

Basophils

1

0.3

0

0.0

0

0.0

Atypical Lymphocytes

0

0.0

0

0.0

0

0.0

WBC

26.7

28.5

22.0

366

Nucleated Red Cells

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M. Neutrophils

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I. Neutrophils

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Lymphocytes

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Monocytes

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Eosinophils

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Basophils

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Atypical Lymphocytes

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WBC

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367

Nucleated Red Cells

0

0

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M. Neutrophils

17

6.0

21

5.7

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I. Neutrophils

0

0.0

3

0.8

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Lymphocytes

70

24.8

61

16.5

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Monocytes

10

3.5

14

3.8

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Eosinophils

3

1.1

1

0.3

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Basophils

0

0.0

0

0.0

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Atypical Lymphocytes

0

0.0

0

0.0

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WBC

35.4

27.1

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368

Nucleated Red Cells

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M. Neutrophils

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I. Neutrophils

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Lymphocytes

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Monocytes

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Eosinophils

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Basophils

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Atypical Lymphocytes

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WBC

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(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 4-M : 4.5 mg base/kg/day

SEX: MALE

ANIMAL ID

WEEK 5

WEEK 9

WEEK 13

REL

ABS

REL

ABS

REL

ABS

369

Nucleated Red Cells

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M. Neutrophils

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I. Neutrophils

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Lymphocytes

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Monocytes

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Eosinophils

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Basophils

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Atypical Lymphocytes

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WBC

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370

Nucleated Red Cells

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M. Neutrophils

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I. Neutrophils

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Lymphocytes

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Monocytes

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Eosinophils

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Basophils

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Atypical Lymphocytes

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WBC

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(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 107

SEX: MALE

GROUP: 1-M : 0 mg base/kg/day

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
301	Polychromasia,Slight Poikilocytes,Mod. to Marked	Poikilocytes,Slight	Polychromasia,Slight Anisocytosis,Slight
302	Poikilocytes,Marked; Target Cells, Moderate	Anisocytosis, Moderate; Polychromasia, Moderate; Poikilocytes,Slight	Normal Red Blood Cells
303	Polychromasia,Slight Poikilocytes, Moderate;Macrocytes, Slight	Anisocytosis, Moderate; Polychromasia,Slight Poikilocytes,Slight	Poikilocytes, Moderate
304	Poikilocytes, Moderate; Anisocytosis, Moderate	Polychromasia,Slight Poikilocytes, Moderate	Polychromasia, Moderate; Poikilocytes,Slight; Anisocytosis, Moderate
305	Polychromasia,Slight Poikilocytes,Marked	Normal Red Blood Cells	Poikilocytes, Moderate; Anisocytosis, Moderate
306	Poikilocytes,Slight	Polychromasia,Slight	Polychromasia,Slight Poikilocytes,Slight
307	Polychromasia,Slight Poikilocytes, Moderate;Macrocytes, Slight	Polychromasia,Slight Poikilocytes,Slight	Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight
308	Polychromasia,Slight Poikilocytes, Moderate	Polychromasia,Slight	Poikilocytes,Mod. to Marked
309	Polychromasia,Slight Poikilocytes,Slight; Macrocytes,Slight	Polychromasia,Slight Macrocytes,Slight; Poikilocytes,Slight	Poikilocytes,Slight; Anisocytosis,Slight

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 107

SEX: MALE

GROUP: 1-M : 0 mg base/kg/day

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
310	Polychromasia,Slight Poikilocytes, Moderate;Macrocytes, Slight	Anisocytosis,Slight; Poikilocytes,Slight	Poikilocytes,Slight; Polychromasia,Slight Anisocytosis,Slight

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 107

SEX: MALE

GROUP: 2-M : 0.5 mg base/kg/day

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
321	--	Poikilocytes, Moderate	Polychromasia,Slight Poikilocytes,Slight
322	Polychromasia, Moderate; Poikilocytes,Slight; Target Cells,Slight	Normal Red Blood Cells	Polychromasia,Slight Poikilocytes,Slight
323	Polychromasia,Slight Poikilocytes,Mod. to Marked;Target Cells, Slight;Macrocytes, Slight	Normal Red Blood Cells	Polychromasia,Slight Poikilocytes,Mod. to Marked;Macrocytes, Slight
324	--	Polychromasia,Slight Poikilocytes,Slight	Polychromasia, Moderate;Macrocytes, Moderate
325	Poikilocytes,Slight	Anisocytosis,Slight; Poikilocytes,Slight	Anisocytosis,Slight
326	Polychromasia,Slight Target Cells,Slight; Macrocytes,Slight	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Poikilocytes, Moderate; Anisocytosis, Moderate
327	Polychromasia, Moderate; Poikilocytes,Slight; Macrocytes,Moderate	Poikilocytes, Moderate	Polychromasia,Slight Poikilocytes, Moderate;Macrocytes, Slight
328	--	Normal Red Blood Cells	Poikilocytes, Moderate
329	Polychromasia,Slight Poikilocytes, Moderate	Anisocytosis,Slight; Polychromasia,Slight Poikilocytes,Slight	Poikilocytes,Mod. to Marked

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 107

SEX: MALE

GROUP: 2-M : 0.5 mg base/kg/day

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
330	Poikilocytes,Slight; Anisocytosis,Slight	Poikilocytes,Slight	Polychromasia,Slight Anisocytosis,Slight

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

MORPHOLOGY OBSERVATIONS

STUDY ID: 107

SEX: MALE

GROUP: 3-M : 1.5 mg base/kg/day

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
341	Polychromasia,Slight Macrocytes,Slight	Polychromasia,Slight Macrocytes,Slight	Polychromasia,Slight Anisocytosis, Moderate
342	Poikilocytes, Moderate; Anisocytosis,Slight	Polychromasia,Slight Macrocytes,Mod. to Marked;Target Cells, Slight	Polychromasia,Slight Anisocytosis,Slight; Toxic Granule,Slight
343	Polychromasia, Moderate;Macrocytes, Moderate	Polychromasia, Moderate;Macrocytes, Moderate; Poikilocytes,Slight	Normal Red Blood Cells
344	Polychromasia,Slight Poikilocytes,Mod. to Marked;Macrocytes, Slight	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight
345	Polychromasia, Moderate; Poikilocytes,Slight; Anisocytosis,Slight; Macrocytes,Moderate	Polychromasia,Slight Macrocytes,Slight	Polychromasia, Moderate; Poikilocytes,Slight; Anisocytosis,Slight
346	Polychromasia,Slight Poikilocytes, Moderate	Anisocytosis,Slight; Polychromasia, Moderate; Poikilocytes,Slight	Polychromasia,Slight Anisocytosis, Moderate
347	Poikilocytes,Mod. to Marked	Polychromasia,Slight	Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight
348	Poikilocytes,Mod. to Marked	Polychromasia,Slight Target Cells,Slight	Polychromasia, Moderate; Anisocytosis, Moderate

(--)-Data Unavailable

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 107

SEX: MALE

GROUP: 3-M : 1.5 mg base/kg/day

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
349	--	Polychromasia,Slight	Polychromasia,Slight Poikilocytes,Slight
350	Polychromasia, Moderate;Macrocytes, Moderate	Polychromasia, Moderate	Polychromasia, Moderate; Poikilocytes,Slight

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 107

SEX: MALE

GROUP: 4-M : 4.5 mg base/kg/day

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
361	--	--	--
362	Polychromasia,Slight Poikilocytes, Moderate;Vacuoles, Slight	Polychromasia, Moderate; Poikilocytes, Moderate	Polychromasia,Mod. to Marked; Poikilocytes,Slight
363	--	--	--
364	Poikilocytes, Moderate; Anisocytosis,Slight	Anisocytosis,Slight; Polychromasia,Slight Poikilocytes, Moderate	Polychromasia,Slight Macrocytes,Slight
365	Polychromasia,Slight Anisocytosis,Slight	Polychromasia, Moderate;Macrocytes, Moderate	Polychromasia, Moderate; Poikilocytes, Moderate
366	--	--	--
367	Poikilocytes,Mod. to Marked	Polychromasia, Moderate;Macrocytes, Moderate	--
368	--	--	--
369	--	--	--
370	--	--	--

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Erythrocytes

STUDY ID: 107
STUDY NO: 107
ABBR: RBC

SEX: FEMALE

UNITS: $10^6/\text{cmm}$

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
GROUP: 1-F:0 mg base/kg/day			
311	7.21	7.59	7.97
312	7.27	7.68	7.97
313	7.75	7.66	7.90
314	7.58	7.90	7.86
315	8.22	8.40	8.59
316	7.14	7.56	7.91
317	7.72	8.28	8.57
318	7.51	8.09	8.20
319	7.13	7.92	8.00
320	7.20	7.99	7.85
MEAN	7.47	7.91	8.08
SD	0.353	0.290	0.280
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day			
331	6.69	7.25	6.77
332	7.84	8.42	8.13
333	6.80	7.65	7.75
334	7.27	7.71	8.28
335	6.94	7.37	7.30
336	7.20	7.56	7.59
337	6.82	7.87	7.76
338	7.57	7.69	8.44
339	7.29	7.70	7.25
340	7.20	8.04	7.51
MEAN	7.16	7.73	7.68
SD	0.362	0.332	0.511
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

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INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Erythrocytes

STUDY ID: 107
STUDY NO: 107
ABBR: RBC

SEX: FEMALE

UNITS: 10⁶/cmm

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	7.16	7.45	7.57
352	6.88	6.79	6.92
353	6.71	6.70	6.64
354	7.41	7.47	7.54
355	7.25	6.87	7.37
356	7.27	7.32	7.59
357	7.25	7.51	7.65
358	6.90	6.82	7.13
359	7.22	7.36	7.57
360	7.27	7.52	7.48

MEAN	7.13	7.18	7.35
SD	0.223	0.340	0.339
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	6.69	6.48	6.77
372	6.61	6.61	6.65
373	6.23	6.54	6.73
374	6.56	6.36	6.54
375	5.99	6.52	6.45
376	6.38	6.23	6.19
377	6.88	6.52	6.95
378	6.94	6.92	6.71
379	6.51	6.63	6.34
380	6.14	6.26	6.43

MEAN	6.49	6.51	6.58
SD	0.310	0.199	0.228
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Hemoglobin

STUDY ID: 107
STUDY NO: 107
ABBR: HGB

SEX: FEMALE

UNITS: g/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	15.5	15.9	16.3
312	15.9	15.8	15.8
313	16.1	16.7	15.4
314	16.1	16.2	15.9
315	17.2	16.8	16.5
316	16.0	16.4	16.3
317	16.9	17.1	16.3
318	16.6	17.0	16.6
319	15.6	16.7	16.9
320	15.0	16.6	15.4

MEAN	16.1	16.5	16.1
SD	0.66	0.44	0.50
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	15.9	16.0	14.6
332	15.9	16.8	16.1
333	14.6	16.2	15.8
334	15.6	16.5	16.1
335	14.7	16.0	15.1
336	15.9	16.1	15.8
337	14.4	16.0	15.4
338	15.7	16.0	16.4
339	15.0	15.9	14.8
340	16.2	16.1	15.2

MEAN	15.4	16.2	15.5
SD	0.65	0.28	0.60
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Hemoglobin

STUDY ID: 107
STUDY NO: 107
ABBR: HGB

SEX: FEMALE

UNITS: g/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	15.7	15.5	16.3
352	14.9	15.2	15.0
353	14.7	13.9	14.5
354	15.8	15.6	15.4
355	15.7	14.9	15.3
356	15.5	15.4	15.5
357	14.6	14.5	14.6
358	15.0	14.4	15.1
359	15.4	15.3	15.3
360	16.3	15.7	15.8

MEAN	15.4	15.0	15.3
SD	0.55	0.60	0.53
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	14.7	14.3	13.9
372	14.8	14.0	14.3
373	14.3	14.4	14.3
374	15.1	14.7	14.4
375	13.7	14.1	14.4
376	14.1	13.8	13.5
377	15.4	14.4	15.0
378	14.9	14.5	13.8
379	14.4	14.2	13.5
380	13.6	13.3	13.2

MEAN	14.5	14.2	14.0
SD	0.59	0.40	0.55
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Hematocrit

STUDY ID: 107
STUDY NO: 107
ABBR: HCT

SEX: FEMALE

UNITS: %

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	41.7	43.9	44.5
312	42.4	44.0	45.4
313	43.4	41.9	42.6
314	42.1	44.2	43.2
315	46.0	46.9	46.5
316	41.6	43.9	44.5
317	44.6	46.7	46.4
318	43.7	46.0	45.5
319	41.3	46.3	47.0
320	40.0	44.8	42.2

MEAN	42.7	44.9	44.8
SD	1.76	1.59	1.68
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	41.9	44.8	41.2
332	43.7	46.8	44.3
333	39.4	44.4	44.6
334	41.3	43.6	45.1
335	41.0	44.1	42.3
336	42.5	44.2	43.6
337	39.4	44.7	43.7
338	42.6	43.8	46.0
339	41.8	45.3	41.3
340	41.6	45.2	42.1

MEAN	41.5	44.7	43.4
SD	1.35	0.93	1.64
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Hematocrit

STUDY ID: 107
STUDY NO: 107
ABBR: HCT

SEX: FEMALE

UNITS: %

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	42.2	43.7	44.5
352	42.4	41.8	42.4
353	40.5	39.7	39.4
354	43.6	43.6	43.0
355	43.4	40.7	43.0
356	42.1	43.3	43.0
357	40.8	41.4	41.7
358	41.4	39.9	40.7
359	41.2	41.2	42.5
360	43.4	43.8	43.3

MEAN	42.1	41.9	42.4
SD	1.12	1.59	1.44
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	40.9	38.9	39.5
372	41.6	40.6	41.1
373	38.7	39.3	40.0
374	43.1	41.5	42.1
375	38.5	40.4	40.1
376	40.6	39.4	38.6
377	44.0	42.1	44.4
378	41.4	39.4	38.5
379	40.9	41.0	38.7
380	38.4	38.7	39.0

MEAN	40.8	40.1	40.2
SD	1.89	1.16	1.88
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

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INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Mean Corpuscular Volume

STUDY ID: 107
STUDY NO: 107
ABBR: MCV

SEX: FEMALE

UNITS: fL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	57.8	57.8	55.8
312	58.3	57.3	57.0
313	56.0	54.7	53.9
314	55.5	55.9	55.0
315	56.0	55.8	54.1
316	58.3	58.1	56.3
317	57.8	56.4	54.1
318	58.2	56.9	55.5
319	57.9	58.5	58.8
320	55.6	56.1	53.8

MEAN	57.1	56.8	55.4
SD	1.20	1.19	1.61
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	62.6	61.8	60.9
332	55.7	55.6	54.5
333	57.9	58.0	57.5
334	56.8	56.5	54.5
335	59.1	59.8	57.9
336	59.0	58.5	57.4
337	57.8	56.8	56.3
338	56.3	57.0	54.5
339	57.3	58.8	57.0
340	57.8	56.2	56.1

MEAN	58.0	57.9	56.7
SD	1.93	1.89	1.98
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Mean Corpuscular Volume

STUDY ID: 107
STUDY NO: 107
ABBR: MCV

SEX: FEMALE

UNITS: fL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	58.9	58.7	58.8
352	61.6	61.6	61.3
353	60.4	59.3	59.3
354	58.8	58.4	57.0
355	59.9	59.2	58.3
356	57.9	59.2	56.7
357	56.3	55.1	54.5
358	60.0	58.5	57.1
359	57.1	56.0	56.1
360	59.7	58.2	57.9

MEAN	59.1	58.4	57.7
SD	1.60	1.80	1.88
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	61.1	60.0	58.3
372	62.9	61.4	61.8
373	62.1	60.1	59.4
374	65.7	65.3	64.4
375	64.3	62.0	62.2
376	63.6	63.2	62.4
377	64.0	64.6	63.9
378	59.7	56.9	57.4
379	62.8	61.8	61.0
380	62.5	61.8	60.7

MEAN	62.9	61.7	61.2
SD	1.69	2.41	2.28
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Mean Corpuscular Hemoglobin

STUDY ID: 107
STUDY NO: 107
ABBR: MCH

SEX: FEMALE

UNITS: pg

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 1-F:0 mg base/kg/day

311	21.5	20.9	20.5
312	21.9	20.6	19.8
313	20.8	20.5	19.5
314	21.2	20.5	20.2
315	20.9	20.0	19.2
316	22.4	21.7	20.6
317	21.9	20.7	19.0
318	22.1	21.0	20.2
319	21.9	21.1	21.1
320	20.8	20.8	19.6

MEAN	21.5	20.8	20.0
SD	0.58	0.45	0.67
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	23.8	22.1	21.6
332	20.3	20.0	19.8
333	21.5	21.2	20.4
334	21.5	21.4	19.4
335	21.2	21.7	20.7
336	22.1	21.3	20.8
337	21.1	20.3	19.8
338	20.7	20.8	19.4
339	20.6	20.6	20.4
340	22.5	20.0	20.2

MEAN	21.5	20.9	20.3
SD	1.04	0.72	0.69
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Mean Corpuscular Hemoglobin

STUDY ID: 107
STUDY NO: 107
ABBR: MCH

SEX: FEMALE

UNITS: pg

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	21.9	20.8	21.5
352	21.7	22.4	21.7
353	21.9	20.7	21.8
354	21.3	20.9	20.4
355	21.7	21.7	20.8
356	21.3	21.0	20.4
357	20.1	19.3	19.1
358	21.7	21.1	21.2
359	21.3	20.8	20.2
360	22.4	20.9	21.1

MEAN	21.5	21.0	20.8
SD	0.61	0.78	0.82
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	22.0	22.1	20.5
372	22.4	21.2	21.5
373	23.0	22.0	21.2
374	23.0	23.1	22.0
375	22.9	21.6	22.3
376	22.1	22.2	21.8
377	22.4	22.1	21.6
378	21.5	21.0	20.6
379	22.1	21.4	21.3
380	22.1	21.2	20.5

MEAN	22.4	21.8	21.3
SD	0.49	0.63	0.64
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Mean Corpus. Hemo. Conc.

STUDY ID: 107
STUDY NO: 107
ABBR: MCHC

SEX: FEMALE

UNITS: g/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	37.2	36.2	36.6
312	37.5	35.9	34.8
313	37.1	37.5	36.2
314	38.2	36.7	36.8
315	37.4	35.8	35.5
316	38.5	37.4	36.6
317	37.9	36.6	35.1
318	38.0	37.0	36.5
319	37.8	36.1	36.0
320	37.5	37.1	36.5

MEAN	37.7	36.6	36.1
SD	0.45	0.61	0.70
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	37.9	35.7	35.4
332	36.4	35.9	36.3
333	37.1	36.5	35.4
334	37.8	37.8	35.7
335	35.9	36.3	35.7
336	37.4	36.4	36.2
337	36.5	35.8	35.2
338	36.9	36.5	35.7
339	35.9	35.1	35.8
340	38.9	35.6	36.1

MEAN	37.1	36.2	35.8
SD	0.96	0.73	0.36
N	10	10	10

LABCAT HE4.26

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THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATSINDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Mean Corpus. Hemo. Conc.STUDY ID: 107
STUDY NO: 107
ABBR: MCHC

SEX: FEMALE

UNITS: g/dL

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	37.2	35.5	36.6
352	35.1	36.4	35.4
353	36.3	35.0	36.8
354	36.2	35.8	35.8
355	36.2	36.6	35.6
356	36.8	35.6	36.0
357	35.8	35.0	35.0
358	36.2	36.1	37.1
359	37.4	37.1	36.0
360	37.6	35.8	36.5

MEAN	36.5	35.9	36.1
SD	0.77	0.68	0.66
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	35.9	36.8	35.2
372	35.6	34.5	34.8
373	37.0	36.6	35.8
374	35.0	35.4	34.2
375	35.6	34.9	35.9
376	34.7	35.0	35.0
377	35.0	34.2	33.8
378	36.0	36.8	35.8
379	35.2	34.6	34.9
380	35.4	34.4	33.8

MEAN	35.5	35.3	34.9
SD	0.66	1.03	0.79
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Reticulocyte Count

STUDY ID: 107
ABBR: RETICS

SEX: FEMALE
UNITS: %RBCs

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 1-F:0 mg base/kg/day

311	0.1	0.2	0.6
312	0.1	0.2	0.6
313	0.7	0.2	0.9
314	0.1	0.4	0.4
315	0.2	0.4	1.3
316	0.8	0.2	1.0
317	0.4	0.5	0.9
318	0.0	0.1	0.6
319	0.5	0.8	0.4
320	0.5	0.3	0.4

MEAN	0.3	0.3	0.7
SD	0.28	0.21	0.30
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	0.2	0.1	1.5
332	0.9	0.3	0.3
333	0.1	0.2	0.6
334	0.5	0.2	0.4
335	0.1	0.3	0.3
336	0.3	0.0	0.6
337	0.1	0.6	0.7
338	0.2	0.7	1.0
339	1.0	0.8	1.0
340	0.5	0.2	0.5

MEAN	0.4	0.3	0.7
SD	0.33	0.27	0.38
N	10	10	10

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Reticulocyte Count

STUDY ID: 107
ABBR: RETICS

SEX: FEMALE
UNITS: %RBCs

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	0.8	2.4	0.6
352	2.7	2.4	1.0
353	0.8	0.9	1.1
354	2.6	0.9	1.2
355	0.7	1.1	0.8
356	0.4	0.7	0.9
357	1.1	1.1	0.2
358	0.8	2.5	0.6
359	0.6	0.7	0.3
360	0.9	0.2	0.6

MEAN	1.1	1.3	0.7
SD	0.82	0.83	0.33
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	4.3	5.4	2.7
372	2.2	3.5	3.6
373	1.9	2.6	2.8
374	3.6	1.9	3.1
375	2.6	3.7	2.4
376	1.2	3.3	4.1
377	1.9	3.7	4.5
378	2.0	3.0	4.4
379	2.2	6.3	4.3
380	3.2	2.6	3.0

MEAN	2.5	3.6	3.5
SD	0.93	1.33	0.79
N	10	10	10

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Nucleated Red Cells

STUDY ID: 107
STUDY NO: 107
ABBR: NRBC

SEX: FEMALE

UNITS: COUNT

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
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GROUP: 1-F:0 mg base/kg/day

311	0	0	0
312	0	0	0
313	0	0	0
314	0	0	0
315	0	0	0
316	0	0	0
317	0	0	0
318	0	0	0
319	0	0	0
320	0	0	0

MEAN	0	0	0
SD	0.0	0.0	0.0
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	0	0	0
332	0	0	0
333	0	0	0
334	0	0	0
335	0	0	0
336	0	0	0
337	0	0	0
338	0	0	0
339	0	0	0
340	0	0	0

MEAN	0	0	0
SD	0.0	0.0	0.0
N	10	10	10

WBC corrected for NRBC = or > 10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Nucleated Red Cells

STUDY ID: 107
STUDY NO: 107
ABBR: NRBC

SEX: FEMALE

UNITS: COUNT

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
-----------	--------	--------	---------

GROUP: 3-F:1.5 mg base/kg/day

351	0	0	0
352	0	0	0
353	0	0	0
354	0	0	0
355	0	0	0
356	0	0	0
357	0	0	0
358	0	0	0
359	0	0	0
360	0	0	0

MEAN	0	0	0
SD	0.0	0.0	0.0
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	0	0	0
372	0	0	0
373	0	0	0
374	0	0	0
375	0	0	0
376	0	0	0
377	0	0	0
378	0	0	0
379	0	0	0
380	0	0	0

MEAN	0	0	0
SD	0.0	0.0	0.0
N	10	10	10

WBC corrected for NRBC = or > 10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Heinz Bodies

STUDY ID: 107
STUDY NO: 107
ABBR: HB

SEX: FEMALE

UNITS: %

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
-----------	--------	--------	---------

GROUP: 1-F:0 mg base/kg/day

311	0.0	0.0	0.0
312	0.0	0.0	0.0
313	0.0	0.0	0.1
314	0.0	0.0	0.0
315	0.0	0.0	0.2
316	0.0	0.0	0.1
317	0.0	0.0	0.0
318	0.0	0.0	0.1
319	0.0	0.1	0.0
320	0.0	0.0	0.0

MEAN	0.0	0.0	0.1
SD	0.00	0.03	0.07
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	0.0	0.0	0.8
332	0.0	0.0	0.0
333	0.0	0.0	0.0
334	0.0	0.0	0.0
335	0.0	0.0	0.0
336	0.0	0.0	0.0
337	0.0	0.0	0.0
338	0.0	0.0	0.5
339	0.0	0.0	0.0
340	0.0	0.0	0.0

MEAN	0.0	0.0	0.1
SD	0.00	0.00	0.28
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Heinz Bodies

STUDY ID: 107
STUDY NO: 107
ABBR: HB

SEX: FEMALE

UNITS: %

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	0.1	0.4	0.1
352	0.0	0.2	0.5
353	0.3	0.2	0.0
354	0.1	0.8	0.2
355	0.0	0.3	0.2
356	0.0	0.0	0.0
357	0.1	0.0	0.0
358	0.3	0.3	0.0
359	0.1	0.1	0.1
360	0.3	0.0	0.2

MEAN	0.1	0.2	0.1
SD	0.13	0.25	0.16
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	0.7	0.7	0.5
372	1.4	1.2	0.6
373	0.4	1.5	1.5
374	0.6	0.2	1.3
375	1.9	2.2	0.6
376	0.6	2.0	2.3
377	0.0	0.9	0.5
378	1.5	0.6	1.3
379	0.5	1.2	1.3
380	2.3	1.5	2.3

MEAN	1.0	1.2	1.2
SD	0.74	0.63	0.69
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: % Methemoglobin

STUDY ID: 107
STUDY NO: 107
ABBR: %METHGB

SEX: FEMALE

UNITS: %

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	1.3	0.6	0.6
312	0.8	0.7	0.8
313	0.7	0.8	1.0
314	0.9	1.0	0.5
315	0.7	1.0	1.0
316	0.7	0.7	0.8
317	0.6	0.6	0.8
318	0.7	1.0	0.6
319	1.1	1.6	0.5
320	0.6	0.8	0.8

MEAN	0.8	0.9	0.7
SD	0.23	0.30	0.18
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	1.5	1.1	1.7
332	1.7	1.3	1.2
333	1.9	1.5	1.2
334	1.6	1.5	1.6
335	1.9	2.2	1.7
336	1.7	1.5	1.6
337	1.3	1.2	1.6
338	1.0	4.5	1.3
339	2.3	1.5	2.1
340	1.8	1.2	1.3

MEAN	1.7	1.8	1.5
SD	0.36	1.01	0.28
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: % Methemoglobin

STUDY ID: 107
STUDY NO: 107
ABBR: %METHGB

SEX: FEMALE

UNITS: %

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	5.2	8.5	8.0
352	4.3	6.4	6.3
353	3.9	4.9	5.3
354	3.9	5.5	7.1
355	2.7	6.3	5.9
356	5.0	5.8	7.3
357	4.1	4.3	6.5
358	5.7	6.3	7.1
359	3.4	5.4	5.6
360	3.5	4.6	5.4

MEAN	4.2	5.8	6.5
SD	0.91	1.20	0.91
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	11.4	16.5	16.8
372	14.0	16.7	15.4
373	11.9	13.4	12.9
374	10.3	13.8	8.2
375	13.5	13.9	15.8
376	11.9	10.5	13.4
377	6.5	11.1	11.5
378	12.7	15.8	16.3
379	12.7	16.4	14.8
380	10.6	11.3	12.0

MEAN	11.6	13.9	13.7
SD	2.13	2.38	2.66
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Platelets

STUDY ID: 107
STUDY NO: 107
ABBR: PLT

SEX: FEMALE

UNITS: 10³/ccm

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	1387	1250	1251
312	1271	1192	1242
313	1383	1280	1229
314	1300	1172	1148
315	1279	1173	1140
316	1264	1064	1024
317	1202	1244	1124
318	1180	1180	1112
319	1329	1228	1213
320	993	948	1089
MEAN	1259	1173	1157
SD	115.1	99.1	74.7
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	858	816	789
332	1157	1069	1106
333	1033	961	1059
334	1117	891	1177
335	1093	1057	911
336	939	968	884
337	1182	1213	800
338	1189	1048	1133
339	986	1072	930
340	1210	1177	1248
MEAN	1076	1027	1004
SD	118.7	121.6	161.9
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Platelets

STUDY ID: 107
STUDY NO: 107
ABBR: PLT

SEX: FEMALE

UNITS: $10^3/\text{ccm}$

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	968	1151	866
352	1352	1223	1129
353	1090	1000	927
354	1263	1238	1073
355	999	1035	915
356	876	1120	990
357	1043	887	991
358	1025	909	930
359	1155	1161	946
360	1036	945	877

MEAN	1081	1067	964
SD	141.5	129.1	83.6
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	983	911	892
372	1105	916	1007
373	978	992	966
374	1123	918	1024
375	1103	1121	986
376	843	944	1000
377	1117	1060	1033
378	972	1086	1037
379	990	934	806
380	1223	1084	1076

MEAN	1044	997	983
SD	109.2	82.9	79.2
N	10	10	10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Leukocytes

STUDY ID: 107
STUDY NO: 107
ABBR: WBC

SEX: FEMALE

UNITS: $10^3/\text{ccm}$

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 1-F:0 mg base/kg/day

311	14.7	10.9	10.8
312	14.0	11.1	7.7
313	12.1	10.0	10.5
314	12.6	19.1	6.3
315	15.5	11.0	10.9
316	12.8	8.8	8.5
317	16.5	19.6	12.8
318	19.1	17.5	15.3
319	16.6	13.6	11.2
320	14.3	9.8	12.8

MEAN	14.8	13.1	10.7
SD	2.16	4.08	2.66
N	10	10	10

GROUP: 2-F:0.5 mg base/kg/day

331	14.5	10.4	9.8
332	14.6	8.6	7.3
333	15.9	13.7	13.6
334	23.5	22.4	19.8
335	14.3	11.6	9.0
336	11.2	10.4	5.9
337	6.5	7.9	7.9
338	12.3	11.7	9.4
339	9.8	8.1	10.3
340	20.2	13.1	10.7

MEAN	14.3	11.8	10.4
SD	4.91	4.23	3.92
N	10	10	10

WBC corrected for NRBC = or > 10

LABCAT HE4.26

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ANIMAL REPORT BY GROUP
TEST: Leukocytes

STUDY ID: 107
STUDY NO: 107
ABBR: WBC

SEX: FEMALE

UNITS: $10^3/\text{ccm}$

ANIMAL ID WEEK 5 WEEK 9 WEEK 13

GROUP: 3-F:1.5 mg base/kg/day

351	18.2	13.6	15.3
352	21.0	17.8	18.1
353	19.4	13.4	14.8
354	21.9	20.0	22.0
355	19.0	15.5	14.9
356	22.0	18.4	19.1
357	12.3	12.5	10.0
358	18.2	10.5	13.5
359	10.2	9.9	4.0
360	17.0	13.4	12.1

MEAN	17.9	14.5	14.4
SD	3.91	3.36	5.04
N	10	10	10

GROUP: 4-F:4.5 mg base/kg/day

371	28.5	19.5	22.0
372	25.9	26.0	20.7
373	32.8	31.7	27.8
374	22.2	17.9	17.6
375	27.7	31.5	25.1
376	34.1	24.5	35.2
377	30.4	31.9	33.8
378	22.0	19.4	14.2
379	27.7	20.9	18.1
380	23.4	20.4	18.0

MEAN	27.5	24.4	23.3
SD	4.20	5.60	7.10
N	10	10	10

WBC corrected for NRBC = or > 10

LABCAT HE4.26

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

WHITE DIFFERENTIAL DATA

STUDY ID: 107
STUDY NO: 107

GROUP: 1-F : 0 mg base/kg/day

SEX: FEMALE

ANIMAL ID		WEEK 5		WEEK 9		WEEK 13	
		REL	ABS	REL	ABS	REL	ABS
311	Nucleated Red Cells	0		0		0	
	M. Neutrophils	14	2.1	8	0.9	9	1.0
	I. Neutrophils	2	0.3	1	0.1	0	0.0
	Lymphocytes	80	11.8	89	9.7	85	9.2
	Monocytes	2	0.3	2	0.2	6	0.6
	Eosinophils	2	0.3	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		14.7		10.9		10.8
312	Nucleated Red Cells	0		0		0	
	M. Neutrophils	14	2.0	13	1.4	18	1.4
	I. Neutrophils	0	0.0	0	0.0	0	0.0
	Lymphocytes	77	10.8	85	9.4	79	6.1
	Monocytes	5	0.7	0	0.0	0	0.0
	Eosinophils	4	0.6	2	0.2	3	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		14.0		11.1		7.7
313	Nucleated Red Cells	0		0		0	
	M. Neutrophils	16	1.9	26	2.6	28	2.9
	I. Neutrophils	2	0.2	5	0.5	2	0.2
	Lymphocytes	76	9.2	60	6.0	64	6.7
	Monocytes	5	0.6	6	0.6	5	0.5
	Eosinophils	1	0.1	3	0.3	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		12.1		10.0		10.5
314	Nucleated Red Cells	0		0		0	
	M. Neutrophils	15	1.9	49	9.4	13	0.8
	I. Neutrophils	1	0.1	1	0.2	4	0.3
	Lymphocytes	79	10.0	43	8.2	78	4.9
	Monocytes	3	0.4	4	0.8	4	0.3
	Eosinophils	2	0.3	2	0.4	1	0.1
	Basophils	0	0.0	1	0.2	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		12.6		19.1		6.3

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

WHITE DIFFERENTIAL DATA

STUDY ID: 107
STUDY NO: 107

GROUP: 1-F : 0 mg base/kg/day

SEX: FEMALE

ANIMAL ID

WEEK 5

WEEK 9

WEEK 13

REL

ABS

REL

ABS

REL

ABS

315	Nucleated Red Cells	0		0		0	
	M. Neutrophils	9	1.4	13	1.4	15	1.6
	I. Neutrophils	1	0.2	0	0.0	1	0.1
	Lymphocytes	86	13.3	87	9.6	81	8.8
	Monocytes	4	0.6	0	0.0	1	0.1
	Eosinophils	0	0.0	0	0.0	2	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		15.5		11.0		10.9
316	Nucleated Red Cells	0		0		0	
	M. Neutrophils	14	1.8	15	1.3	20	1.7
	I. Neutrophils	1	0.1	0	0.0	2	0.2
	Lymphocytes	81	10.4	78	6.9	77	6.5
	Monocytes	3	0.4	4	0.4	0	0.0
	Eosinophils	1	0.1	3	0.3	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		12.8		8.8		8.5
317	Nucleated Red Cells	0		0		0	
	M. Neutrophils	7	1.2	21	4.1	9	1.2
	I. Neutrophils	0	0.0	0	0.0	1	0.1
	Lymphocytes	92	15.2	77	15.1	87	11.1
	Monocytes	1	0.2	2	0.4	0	0.0
	Eosinophils	0	0.0	0	0.0	3	0.4
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		16.5		19.6		12.8
318	Nucleated Red Cells	0		0		0	
	M. Neutrophils	12	2.3	12	2.1	11	1.7
	I. Neutrophils	0	0.0	0	0.0	1	0.2
	Lymphocytes	86	16.4	88	15.4	84	12.9
	Monocytes	2	0.4	0	0.0	3	0.5
	Eosinophils	0	0.0	0	0.0	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		19.1		17.5		15.3

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 1-F : 0 mg base/kg/day

SEX: FEMALE

ANIMAL ID

WEEK 5

WEEK 9

WEEK 13

REL

ABS

REL

ABS

REL

ABS

319

Nucleated Red Cells

0

0

0

M. Neutrophils

7

1.2

17

2.3

12

1.3

I. Neutrophils

0

0.0

0

0.0

0

0.0

Lymphocytes

91

15.1

79

10.7

88

9.9

Monocytes

2

0.3

3

0.4

0

0.0

Eosinophils

0

0.0

1

0.1

0

0.0

Basophils

0

0.0

0

0.0

0

0.0

Atypical Lymphocytes

0

0.0

0

0.0

0

0.0

WBC

16.6

13.6

11.2

320

Nucleated Red Cells

0

0

0

M. Neutrophils

2

0.3

12

1.2

23

2.9

I. Neutrophils

2

0.3

0

0.0

3

0.4

Lymphocytes

92

13.2

87

8.5

67

8.6

Monocytes

4

0.6

1

0.1

6

0.8

Eosinophils

0

0.0

0

0.0

1

0.1

Basophils

0

0.0

0

0.0

0

0.0

Atypical Lymphocytes

0

0.0

0

0.0

0

0.0

WBC

14.3

9.8

12.8

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 2-F : 0.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID

WEEK 5

WEEK 9

WEEK 13

REL

ABS

REL

ABS

REL

ABS

331	Nucleated Red Cells	0		0		0	
	M. Neutrophils	81	11.7	7	0.7	9	0.9
	I. Neutrophils	0	0.0	0	0.0	2	0.2
	Lymphocytes	11	1.6	89	9.3	87	8.5
	Monocytes	5	0.7	2	0.2	1	0.1
	Eosinophils	3	0.4	2	0.2	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		14.5		10.4		9.8
332	Nucleated Red Cells	0		0		0	
	M. Neutrophils	12	1.8	21	1.8	15	1.1
	I. Neutrophils	2	0.3	1	0.1	3	0.2
	Lymphocytes	78	11.4	77	6.6	78	5.7
	Monocytes	5	0.7	0	0.0	2	0.1
	Eosinophils	3	0.4	1	0.1	2	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		14.6		8.6		7.3
333	Nucleated Red Cells	0		0		0	
	M. Neutrophils	23	3.7	18	2.5	14	1.9
	I. Neutrophils	2	0.3	0	0.0	1	0.1
	Lymphocytes	71	11.3	79	10.8	80	10.9
	Monocytes	4	0.6	1	0.1	4	0.5
	Eosinophils	0	0.0	2	0.3	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		15.9		13.7		13.6
334	Nucleated Red Cells	0		0		0	
	M. Neutrophils	12	2.8	18	4.0	28	5.5
	I. Neutrophils	2	0.5	1	0.2	2	0.4
	Lymphocytes	80	18.8	77	17.2	65	12.9
	Monocytes	5	1.2	4	0.9	3	0.6
	Eosinophils	0	0.0	0	0.0	2	0.4
	Basophils	1	0.2	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		23.5		22.4		19.8

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

WHITE DIFFERENTIAL DATA

STUDY ID: 107
STUDY NO: 107

GROUP: 2-F : 0.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID

WEEK 5

WEEK 9

WEEK 13

REL

ABS

REL

ABS

REL

ABS

335	Nucleated Red Cells	0		0		0	
	M. Neutrophils	11	1.6	11	1.3	7	0.6
	I. Neutrophils	1	0.1	1	0.1	1	0.1
	Lymphocytes	85	12.2	88	10.2	83	7.5
	Monocytes	1	0.1	0	0.0	9	0.8
	Eosinophils	2	0.3	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		14.3		11.6		9.0
336	Nucleated Red Cells	0		0		0	
	M. Neutrophils	24	2.7	25	2.6	18	1.1
	I. Neutrophils	0	0.0	5	0.5	0	0.0
	Lymphocytes	72	8.1	68	7.1	74	4.4
	Monocytes	3	0.3	0	0.0	3	0.2
	Eosinophils	1	0.1	2	0.2	5	0.3
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		11.2		10.4		5.9
337	Nucleated Red Cells	0		0		0	
	M. Neutrophils	18	1.2	12	0.9	20	1.6
	I. Neutrophils	0	0.0	1	0.1	1	0.1
	Lymphocytes	76	4.9	84	6.6	76	6.0
	Monocytes	4	0.3	3	0.2	0	0.0
	Eosinophils	2	0.1	0	0.0	3	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		6.5		7.9		7.9
338	Nucleated Red Cells	0		0		0	
	M. Neutrophils	12	1.5	14	1.6	14	1.3
	I. Neutrophils	2	0.2	0	0.0	5	0.5
	Lymphocytes	81	10.0	83	9.7	72	6.8
	Monocytes	4	0.5	3	0.4	3	0.3
	Eosinophils	1	0.1	0	0.0	6	0.6
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		12.3		11.7		9.4

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 2-F : 0.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID

WEEK 5

WEEK 9

WEEK 13

REL

ABS

REL

ABS

REL

ABS

339

Nucleated Red Cells

0

0

0

M. Neutrophils

31

3.0

14

1.1

8

0.8

I. Neutrophils

0

0.0

2

0.2

2

0.2

Lymphocytes

69

6.8

83

6.7

81

8.3

Monocytes

0

0.0

0

0.0

7

0.7

Eosinophils

0

0.0

1

0.1

2

0.2

Basophils

0

0.0

0

0.0

0

0.0

Atypical Lymphocytes

0

0.0

0

0.0

0

0.0

WBC

9.8

8.1

10.3

340

Nucleated Red Cells

0

0

0

M. Neutrophils

14

2.8

25

3.3

9

1.0

I. Neutrophils

2

0.4

3

0.4

4

0.4

Lymphocytes

77

15.6

69

9.0

83

8.9

Monocytes

6

1.2

2

0.3

4

0.4

Eosinophils

1

0.2

1

0.1

0

0.0

Basophils

0

0.0

0

0.0

0

0.0

Atypical Lymphocytes

0

0.0

0

0.0

0

0.0

WBC

20.2

13.1

10.7

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 3-F : 1.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID

WEEK 5
REL ABS

WEEK 9
REL ABS

WEEK 13
REL ABS

351	Nucleated Red Cells	0		0		0	
	M. Neutrophils	13	2.4	9	1.2	14	2.1
	I. Neutrophils	0	0.0	0	0.0	1	0.2
	Lymphocytes	83	15.1	86	11.7	79	12.1
	Monocytes	4	0.7	4	0.5	6	0.9
	Eosinophils	0	0.0	1	0.1	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		18.2		13.6		15.3
352	Nucleated Red Cells	0		0		0	
	M. Neutrophils	11	2.3	14	2.5	20	3.6
	I. Neutrophils	1	0.2	0	0.0	6	1.1
	Lymphocytes	82	17.2	82	14.6	71	12.9
	Monocytes	4	0.8	4	0.7	0	0.0
	Eosinophils	2	0.4	0	0.0	3	0.5
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		21.0		17.8		18.1
353	Nucleated Red Cells	0		0		0	
	M. Neutrophils	17	3.3	17	2.3	18	2.7
	I. Neutrophils	0	0.0	0	0.0	2	0.3
	Lymphocytes	80	15.5	80	10.7	78	11.5
	Monocytes	3	0.6	3	0.4	1	0.1
	Eosinophils	0	0.0	0	0.0	1	0.1
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		19.4		13.4		14.8
354	Nucleated Red Cells	0		0		0	
	M. Neutrophils	17	3.7	9	1.8	14	3.1
	I. Neutrophils	1	0.2	3	0.6	1	0.2
	Lymphocytes	80	17.5	80	16.0	76	16.7
	Monocytes	2	0.4	7	1.4	8	1.8
	Eosinophils	0	0.0	1	0.2	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		21.9		20.0		22.0

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 3-F : 1.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID		WEEK 5		WEEK 9		WEEK 13	
		REL	ABS	REL	ABS	REL	ABS
355	Nucleated Red Cells	0		0		0	
	M. Neutrophils	19	3.6	13	2.0	15	2.2
	I. Neutrophils	0	0.0	2	0.3	6	0.9
	Lymphocytes	75	14.3	82	12.7	79	11.8
	Monocytes	6	1.1	2	0.3	0	0.0
	Eosinophils	0	0.0	1	0.2	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		19.0		15.5		14.9
356	Nucleated Red Cells	0		0		0	
	M. Neutrophils	14	3.1	16	2.9	21	4.0
	I. Neutrophils	0	0.0	0	0.0	3	0.6
	Lymphocytes	85	18.7	81	14.9	74	14.1
	Monocytes	1	0.2	2	0.4	1	0.2
	Eosinophils	0	0.0	1	0.2	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		22.0		18.4		19.1
357	Nucleated Red Cells	0		0		0	
	M. Neutrophils	19	2.3	18	2.3	17	1.7
	I. Neutrophils	0	0.0	3	0.4	0	0.0
	Lymphocytes	79	9.7	74	9.3	78	7.8
	Monocytes	2	0.2	2	0.3	3	0.3
	Eosinophils	0	0.0	3	0.4	2	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		12.3		12.5		10.0
358	Nucleated Red Cells	0		0		0	
	M. Neutrophils	14	2.5	20	2.1	8	1.1
	I. Neutrophils	0	0.0	2	0.2	5	0.7
	Lymphocytes	85	15.5	73	7.7	83	11.2
	Monocytes	1	0.2	2	0.2	4	0.5
	Eosinophils	0	0.0	3	0.3	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		18.2		10.5		13.5

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 3-F : 1.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID

WEEK 5

REL

ABS

WEEK 9

REL

ABS

WEEK 13

REL

ABS

359

Nucleated Red Cells

0

0

0

M. Neutrophils

28

2.9

15

1.5

25

1.0

I. Neutrophils

2

0.2

2

0.2

1

0.0

Lymphocytes

65

6.6

80

7.9

72

2.9

Monocytes

3

0.3

2

0.2

1

0.0

Eosinophils

2

0.2

1

0.1

1

0.0

Basophils

0

0.0

0

0.0

0

0.0

Atypical Lymphocytes

0

0.0

0

0.0

0

0.0

WBC

10.2

9.9

4.0

360

Nucleated Red Cells

0

0

0

M. Neutrophils

15

2.6

14

1.9

26

3.1

I. Neutrophils

2

0.3

2

0.3

5

0.6

Lymphocytes

78

13.3

82

11.0

66

8.0

Monocytes

4

0.7

0

0.0

1

0.1

Eosinophils

1

0.2

2

0.3

2

0.2

Basophils

0

0.0

0

0.0

0

0.0

Atypical Lymphocytes

0

0.0

0

0.0

0

0.0

WBC

17.0

13.4

12.1

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

DRAFT

WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 4-F : 4.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID		WEEK 5		WEEK 9		WEEK 13	
		REL	ABS	REL	ABS	REL	ABS
371	Nucleated Red Cells	0		0		0	
	M. Neutrophils	8	2.3	8	1.6	18	4.0
	I. Neutrophils	1	0.3	0	0.0	4	0.9
	Lymphocytes	89	25.4	89	17.4	76	16.7
	Monocytes	1	0.3	3	0.6	2	0.4
	Eosinophils	1	0.3	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		28.5		19.5		22.0
372	Nucleated Red Cells	0		0		0	
	M. Neutrophils	8	2.1	13	3.4	13	2.7
	I. Neutrophils	0	0.0	2	0.5	1	0.2
	Lymphocytes	85	22.0	81	21.1	77	15.9
	Monocytes	6	1.6	2	0.5	8	1.7
	Eosinophils	1	0.3	2	0.5	1	0.2
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		25.9		26.0		20.7
373	Nucleated Red Cells	0		0		0	
	M. Neutrophils	9	3.0	10	3.2	12	3.3
	I. Neutrophils	0	0.0	3	1.0	5	1.4
	Lymphocytes	89	29.2	80	25.4	81	22.5
	Monocytes	2	0.7	4	1.3	2	0.6
	Eosinophils	0	0.0	3	1.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		32.8		31.7		27.8
374	Nucleated Red Cells	0		0		0	
	M. Neutrophils	16	3.6	10	1.8	19	3.3
	I. Neutrophils	0	0.0	1	0.2	1	0.2
	Lymphocytes	78	17.3	84	15.0	74	13.0
	Monocytes	4	0.9	5	0.9	6	1.1
	Eosinophils	2	0.4	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		22.2		17.9		17.6

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 4-F : 4.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID

WEEK 5

WEEK 9

WEEK 13

REL

ABS

REL

ABS

REL

ABS

375	Nucleated Red Cells	0		0		0	
	M. Neutrophils	18	5.0	14	4.4	12	3.0
	I. Neutrophils	4	1.1	2	0.6	0	0.0
	Lymphocytes	74	20.5	80	25.2	82	20.6
	Monocytes	4	1.1	4	1.3	6	1.5
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		27.7		31.5		25.1
376	Nucleated Red Cells	0		0		0	
	M. Neutrophils	12	4.1	17	4.2	13	4.6
	I. Neutrophils	3	1.0	2	0.5	5	1.8
	Lymphocytes	77	26.3	79	19.4	81	28.5
	Monocytes	6	2.0	2	0.5	1	0.4
	Eosinophils	2	0.7	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		34.1		24.5		35.2
377	Nucleated Red Cells	0		0		0	
	M. Neutrophils	7	2.1	17	5.4	10	3.4
	I. Neutrophils	7	2.1	0	0.0	5	1.7
	Lymphocytes	79	24.0	79	25.2	79	26.7
	Monocytes	5	1.5	3	1.0	5	1.7
	Eosinophils	2	0.6	1	0.3	1	0.3
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		30.4		31.9		33.8
378	Nucleated Red Cells	0		0		0	
	M. Neutrophils	23	5.1	13	2.5	22	3.1
	I. Neutrophils	1	0.2	1	0.2	4	0.6
	Lymphocytes	74	16.3	84	16.3	65	9.2
	Monocytes	2	0.4	2	0.4	9	1.3
	Eosinophils	0	0.0	0	0.0	0	0.0
	Basophils	0	0.0	0	0.0	0	0.0
	Atypical Lymphocytes	0	0.0	0	0.0	0	0.0
	WBC		22.0		19.4		14.2

DRAFT

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

WHITE DIFFERENTIAL DATA

STUDY ID: 107

STUDY NO: 107

GROUP: 4-F : 4.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID

WEEK 5

WEEK 9

WEEK 13

REL

ABS

REL

ABS

REL

ABS

379

Nucleated Red Cells

0

0

0

M. Neutrophils

10

2.8

15

3.1

10

1.8

I. Neutrophils

5

1.4

1

0.2

4

0.7

Lymphocytes

81

22.4

81

16.9

85

15.4

Monocytes

4

1.1

3

0.6

1

0.2

Eosinophils

0

0.0

0

0.0

0

0.0

Basophils

0

0.0

0

0.0

0

0.0

Atypical Lymphocytes

0

0.0

0

0.0

0

0.0

WBC

27.7

20.9

18.1

380

Nucleated Red Cells

0

0

0

M. Neutrophils

23

5.4

15

3.1

28

5.0

I. Neutrophils

1

0.2

0

0.0

2

0.4

Lymphocytes

66

15.4

83

16.9

69

12.4

Monocytes

10

2.3

2

0.4

1

0.2

Eosinophils

0

0.0

0

0.0

0

0.0

Basophils

0

0.0

0

0.0

0

0.0

Atypical Lymphocytes

0

0.0

0

0.0

0

0.0

WBC

23.4

20.4

18.0

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 107

SEX: FEMALE

GROUP: 1-F : 0 mg base/kg/day

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
311	Poikilocytes,Slight; Anisocytosis,Slight	Normal Red Blood Cells	Polychromasia,Slight Poikilocytes,Mod. to Marked
312	--	Polychromasia,Slight Poikilocytes, Moderate	Poikilocytes, Moderate
313	Polychromasia, Moderate; Anisocytosis,Slight	Poikilocytes, Moderate;Target Cells,Mod. to Marked	Polychromasia,Slight Poikilocytes,Mod. to Marked
314	Poikilocytes,Mod. to Marked	Polychromasia,Slight Poikilocytes,Slight	Poikilocytes,Slight
315	Polychromasia,Slight Poikilocytes,Mod. to Marked	Normal Red Blood Cells	Normal Red Blood Cells
316	Poikilocytes, Moderate; Anisocytosis,Slight	Poikilocytes, Moderate	Poikilocytes,Slight
317	Poikilocytes,Mod. to Marked	Poikilocytes, Moderate	Polychromasia,Slight Macrocytes,Slight
318	Polychromasia,Slight Macrocytes,Slight	Normal Red Blood Cells	Normal Red Blood Cells
319	Polychromasia,Slight Poikilocytes,Mod. to Marked;Anisocytosis, Slight	Normal Red Blood Cells	Polychromasia, Moderate; Poikilocytes,Mod. to Marked
320	Poikilocytes,Slight; Anisocytosis,Slight	Normal Red Blood Cells	Normal Red Blood Cells

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 107

GROUP: 2-F : 0.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
331	Poikilocytes,Slight; Anisocytosis,Slight	Poikilocytes,Mod. to Marked	Polychromasia,Slight Poikilocytes,Mod. to Marked
332	Polychromasia,Mod. to Marked; Anisocytosis,Slight	Anisocytosis,Slight; Poikilocytes,Slight	Polychromasia,Slight Poikilocytes, Moderate
333	Poikilocytes,Mod. to Marked;Anisocytosis, Slight	Anisocytosis,Slight; Polychromasia,Slight	Normal Red Blood Cells
334	Polychromasia,Slight Poikilocytes, Moderate;Macrocytes, Slight	Poikilocytes,Mod. to Marked	Polychromasia,Slight Poikilocytes,Mod. to Marked;Macrocytes, Slight
335	Poikilocytes,Mod. to Marked	Normal Red Blood Cells	Polychromasia,Slight Poikilocytes, Moderate; Anisocytosis,Slight
336	Polychromasia,Slight Poikilocytes,Mod. to Marked	Poikilocytes,Slight	Poikilocytes,Slight
337	Polychromasia,Slight Poikilocytes,Slight	Anisocytosis,Slight; Polychromasia,Slight	Poikilocytes,Mod. to Marked
338	Polychromasia,Slight Poikilocytes,Slight; Macrocytes,Slight	Polychromasia, Moderate; Poikilocytes, Moderate	Poikilocytes, Moderate; Anisocytosis,Slight
339	Polychromasia,Slight Poikilocytes, Moderate	Poikilocytes,Mod. to Marked;Target Cells, Slight	Polychromasia, Moderate; Poikilocytes, Moderate; Anisocytosis, Moderate

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 107

GROUP: 2-F : 0.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
340	Poikilocytes, Mod. to Marked	Anisocytosis, Moderate	Normal Red Blood Cells

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 107

GROUP: 3-F : 1.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
351	Polychromasia,Slight Poikilocytes, Moderate	Anisocytosis, Moderate; Polychromasia, Moderate; Poikilocytes,Slight	Polychromasia,Slight Poikilocytes,Slight; Anisocytosis,Slight
352	Polychromasia,Slight Poikilocytes,Mod. to Marked;Macrocytes, Slight	Anisocytosis,Slight; Polychromasia,Mod. to Marked; Poikilocytes,Slight	Polychromasia, Moderate; Poikilocytes,Mod. to Marked
353	Polychromasia,Slight Anisocytosis,Slight	Polychromasia,Slight Macrocytes,Slight	Polychromasia,Slight Poikilocytes, Moderate; Anisocytosis,Slight
354	Polychromasia,Mod. to Marked; Poikilocytes,Slight; Target Cells,Slight; Macrocytes,Slight	Anisocytosis, Moderate	Polychromasia,Slight Poikilocytes,Slight
355	Polychromasia, Moderate; Poikilocytes,Mod. to Marked;Macrocytes, Moderate	Polychromasia,Slight Poikilocytes, Moderate	Poikilocytes, Moderate
356	Poikilocytes,Marked	Normal Red Blood Cells	Normal Red Blood Cells
357	Polychromasia,Slight Poikilocytes,Slight	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia,Slight Poikilocytes,Mod. to Marked;Macrocytes, Slight
358	Poikilocytes,Marked; Anisocytosis,Slight	Anisocytosis,Mod. to Marked;Polychromasia Mod. to Marked; Poikilocytes, Moderate	Polychromasia,Slight Poikilocytes,Marked

(--)-Data Unavailable

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 107

SEX: FEMALE

GROUP: 3-F : 1.5 mg base/kg/day

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
359	--	Polychromasia,Slight Poikilocytes,Mod. to Marked	Normal Red Blood Cells
360	Anisocytosis,Slight; Polychromasia,Slight	Poikilocytes, Moderate	Polychromasia, Moderate

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 107

GROUP: 4-F : 4.5 mg base/kg/day

SEX: FEMALE

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
371	Polychromasia, Moderate; Poikilocytes,Slight; Macrocytes,Moderate	Anisocytosis, Moderate; Polychromasia,Mod. to Marked	Polychromasia, Moderate; Poikilocytes,Slight; Anisocytosis,Slight
372	Poikilocytes,Slight; Anisocytosis, Moderate	Anisocytosis,Slight; Polychromasia,Slight	Polychromasia, Moderate; Poikilocytes,Slight
373	Polychromasia, Moderate; Poikilocytes,Slight; Target Cells,Slight; Anisocytosis,Slight	Polychromasia,Mod. to Marked; Poikilocytes,Slight; Macrocytes,Mod. to Marked	Polychromasia, Moderate;Target Cells,Slight
374	Polychromasia, Moderate;Macrocytes, Slight	Anisocytosis, Moderate; Polychromasia, Moderate	Polychromasia,Mod. to Marked; Poikilocytes,Slight
375	Polychromasia,Slight Poikilocytes, Moderate;Macrocytes, Slight	Polychromasia,Mod. to Marked;Macrocytes Mod. to Marked; Poikilocytes,Slight	Polychromasia,Mod. to Marked; Poikilocytes,Slight; Anisocytosis,Mod. to Marked
376	Poikilocytes,Marked; Anisocytosis,Slight	Anisocytosis, Moderate; Polychromasia,Slight	Polychromasia,Slight Macrocytes,Slight
377	Polychromasia, Moderate; Poikilocytes, Moderate;Macrocytes, Moderate	Polychromasia,Mod. to Marked;Macrocytes Mod. to Marked	Polychromasia,Mod. to Marked
378	Polychromasia,Slight Macrocytes,Slight	Anisocytosis,Mod. to Marked;Polychromasia Mod. to Marked; Poikilocytes, Moderate	Polychromasia,Slight Poikilocytes, Moderate

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

MORPHOLOGY OBSERVATIONS

STUDY ID: 107

SEX: FEMALE

GROUP: 4-F : 4.5 mg base/kg/day

ANIMAL ID	WEEK 5	WEEK 9	WEEK 13
379	Polychromasia,Slight Poikilocytes,Mod. to Marked;Macrocytes, Slight	Polychromasia,Mod. to Marked;Macrocytes Mod. to Marked	Polychromasia, Moderate; Poikilocytes,Mod. to Marked;Macrocytes, Moderate
380	Polychromasia,Slight Poikilocytes, Moderate;Macrocytes, Slight	Polychromasia,Mod. to Marked;Macrocytes Mod. to Marked; Target Cells,Slight	Polychromasia, Moderate;Target Cells,Slight

DRAFT

APPENDIX 8
Ophthalmology Report

ANIMAL EYE ASSOCIATES

DRAFT

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March 29, 1994

OPHTHALMIC REPORT

UIC/TRL Study No. 107

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS

On October 13, 1993, (Week -1), a sufficient number of CD® rats were given ophthalmic examinations by indirect ophthalmoscopy to result in forty males and forty females suitable for the study.

On January 12, 1994 (Week 13), I re-examined the remaining 71 rats. One mid dose male (No. 346) was diagnosed with unilateral generalized retinal degeneration. One low dose female (No. 336) was diagnosed with unilateral retinal hemorrhages. Because ocular lesions were not seen in high dose animals, these findings were considered to be spurious and not a treatment-related effect. All other rats appeared similar (no lesions) to the previous pretest examinations done on October 13, 1993.

Sincerely,



Samuel J. Vainisi, D.V.M.
Professor of Comparative
Ophthalmology, U. of IL. at Chicago

Diplomate, American College of
Veterinary Ophthalmologists

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS

Ophthalmic Examinations
Males

DRAFT

Dose	Animal Number	Week -1		Week 13	
		R.E.	L.E.	R.E.	L.E.
0	301	WNL	WNL	WNL	WNL
	302	WNL	WNL	WNL	WNL
	303	WNL	WNL	WNL	WNL
	304	WNL	WNL	WNL	WNL
	305	WNL	WNL	WNL	WNL
	306	WNL	WNL	WNL	WNL
	307	WNL	WNL	WNL	WNL
	308	WNL	WNL	WNL	WNL
	309	WNL	WNL	WNL	WNL
	310	WNL	WNL	WNL	WNL
0.5	321	WNL	WNL	WNL	WNL
	322	WNL	WNL	WNL	WNL
	323	WNL	WNL	WNL	WNL
	324	WNL	WNL	WNL	WNL
	325	WNL	WNL	WNL	WNL
	326	WNL	WNL	WNL	WNL
	327	WNL	WNL	WNL	WNL
	328	WNL	WNL	*	*
	329	WNL	WNL	WNL	WNL
	330	WNL	WNL	WNL	WNL
1.5	341	WNL	WNL	WNL	WNL
	342	WNL	WNL	*	*
	343	WNL	WNL	WNL	WNL
	344	WNL	WNL	WNL	WNL
	345	WNL	WNL	WNL	WNL
	346	WNL	WNL	WNL	GRD
	347	WNL	WNL	WNL	WNL
	348	WNL	WNL	WNL	WNL
	349	WNL	WNL	WNL	WNL
	350	WNL	WNL	WNL	WNL
4.5	361	WNL	WNL	*	*
	362	WNL	WNL	WNL	WNL
	363	WNL	WNL	*	*
	364	WNL	WNL	WNL	WNL
	365	WNL	WNL	WNL	WNL
	366	WNL	WNL	*	*
	367	WNL	WNL	*	*
	368	WNL	WNL	*	*
	369	WNL	WNL	*	*
	370	WNL	WNL	*	*

Dose = mg base/kg/day

R.E. = Right Eye

L.E. = Left Eye

* = Animal Previously Died

WNL = Within Normal Limits

RH = Retinal Hemorrhage

GRD = Generalized Retinal Degeneration

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS

Ophthalmic Examinations
Females

DRAFT

Dose	Animal Number	Week -1		Week 13	
		R.E.	L.E.	R.E.	L.E.
0	311	WNL	WNL	WNL	WNL
	312	WNL	WNL	WNL	WNL
	313	WNL	WNL	WNL	WNL
	314	WNL	WNL	WNL	WNL
	315	WNL	WNL	WNL	WNL
	316	WNL	WNL	WNL	WNL
	317	WNL	WNL	WNL	WNL
	318	WNL	WNL	WNL	WNL
	319	WNL	WNL	WNL	WNL
	320	WNL	WNL	WNL	WNL
0.5	331	WNL	WNL	WNL	WNL
	332	WNL	WNL	WNL	WNL
	333	WNL	WNL	WNL	WNL
	334	WNL	WNL	WNL	WNL
	335	WNL	WNL	WNL	WNL
	336	WNL	WNL	WNL	RH
	337	WNL	WNL	WNL	WNL
	338	WNL	WNL	WNL	WNL
	339	WNL	WNL	WNL	WNL
	340	WNL	WNL	WNL	WNL
1.5	351	WNL	WNL	WNL	WNL
	352	WNL	WNL	WNL	WNL
	353	WNL	WNL	WNL	WNL
	354	WNL	WNL	WNL	WNL
	355	WNL	WNL	WNL	WNL
	356	WNL	WNL	WNL	WNL
	357	WNL	WNL	WNL	WNL
	358	WNL	WNL	WNL	WNL
	359	WNL	WNL	WNL	WNL
	360	WNL	WNL	WNL	WNL
4.5	371	WNL	WNL	WNL	WNL
	372	WNL	WNL	WNL	WNL
	373	WNL	WNL	WNL	WNL
	374	WNL	WNL	WNL	WNL
	375	WNL	WNL	WNL	WNL
	376	WNL	WNL	WNL	WNL
	377	WNL	WNL	WNL	WNL
	378	WNL	WNL	WNL	WNL
	379	WNL	WNL	WNL	WNL
	380	WNL	WNL	WNL	WNL

Dose = mg base/kg/day

R.E. = Right Eye

L.E. = Left Eye

* = Animal Previously Died

WNL = Within Normal Limits

RH = Retinal Hemorrhage

GRD = Generalized Retinal Degeneration

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APPENDIX 9
Individual Organ Weights

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THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 107
SEX: MALE

GROUP: 1-M - 0 mg base/kg/day
ALL FATES DAYS: 91-92 ALL BALANCES

ANIMAL ID: BALANCE NO.:	301	302	303	304	305	306	307	308	309
BODY WEIGHT (G)	596	623	580	695	574	599	625	604	702
ADRENAL GLANDS (G)	0.077	0.071	0.061	0.063	0.061	0.079	0.062	0.074	0.069
% BRAIN WEIGHT	3.49	3.13	2.57	2.72	2.36	3.61	2.72	3.22	2.80
BRAIN (G)	2.206	2.265	2.373	2.318	2.586	2.189	2.276	2.298	2.466
HEART (G)	1.910	2.288	2.492	2.323	2.088	1.678	1.999	1.870	2.256
% BRAIN WEIGHT	86.58	101.02	105.01	100.22	80.74	76.66	87.83	81.38	91.48
KIDNEYS (G)	4.281	5.164	5.260	5.997	4.949	4.000	5.008	4.881	5.130
% BRAIN WEIGHT	194.06	227.99	221.66	258.71	191.38	182.73	220.04	212.40	208.03
LIVER (G)	19.889	24.948	22.453	24.402	21.583	19.089	22.371	20.014	24.060
% BRAIN WEIGHT	901.59	1101.46	946.19	1052.72	834.61	872.04	982.91	870.93	975.67
SPLEEN (G)	1.059	0.991	0.984	1.001	1.013	0.877	1.121	0.983	1.264
% BRAIN WEIGHT	48.01	43.75	41.47	43.18	39.17	40.06	49.25	42.78	51.26
TESTES WITH EPIDIDYMIDES (G)	5.650	5.871	5.537	5.947	5.618	5.651	5.719	5.899	5.852
% BRAIN WEIGHT	256.12	259.21	233.33	256.56	217.25	258.15	251.27	256.70	237.31

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 107
SEX: MALE

GROUP: 1-M - 0 mg base/kg/day
ALL FATES DAYS: 91-92 ALL BALANCES

ANIMAL ID: 310
BALANCE NO.:

BODY WEIGHT (G) 562

ADRENAL GLANDS (G) 0.054
% BRAIN WEIGHT 2.48

BRAIN (G) 2.175

HEART (G) 1.836
% BRAIN WEIGHT 84.41

KIDNEYS (G) 4.161
% BRAIN WEIGHT 191.31

LIVER (G) 19.800
% BRAIN WEIGHT 910.34

SPLEEN (G) 0.771
% BRAIN WEIGHT 35.45

TESTES WITH EPIDIDYMIDES (G) 5.120
% BRAIN WEIGHT 235.40

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 107

SEX: MALE

GROUP: 2-M - 0.5 mg base/kg/day

ALL FATES

DAYS: 91-92

ALL BALANCES

ANIMAL ID: BALANCE NO.:	321	322	323	324	325	326	327	329	330
BODY WEIGHT (G)	616	648	658	607	606	599	602	630	608
ADRENAL GLANDS (G)	0.061	0.064	0.068	0.062	0.065	0.068	0.065	0.072	0.109
% BRAIN WEIGHT	2.37	2.88	2.86	3.06	2.83	3.04	2.98	3.07	4.57
BRAIN (G)	2.570	2.226	2.375	2.024	2.296	2.236	2.178	2.348	2.385
HEART (G)	1.940	2.076	2.371	2.042	1.788	2.202	1.935	2.377	2.281
% BRAIN WEIGHT	75.49	93.26	99.83	100.89	77.87	98.48	88.84	101.24	95.64
KIDNEYS (G)	5.262	4.865	5.152	5.091	5.015	4.872	4.387	5.178	5.477
% BRAIN WEIGHT	204.75	218.55	216.93	251.53	218.42	217.89	201.42	220.53	229.64
LIVER (G)	22.967	24.267	27.005	22.733	21.893	24.726	21.671	28.528	23.973
% BRAIN WEIGHT	893.66	1090.16	1137.05	1123.17	953.53	1105.81	995.00	1214.99	1005.16
SPLEEN (G)	1.532	1.689	1.797	1.089	1.391	1.242	1.594	1.560	1.356
% BRAIN WEIGHT	59.61	75.88	75.66	53.80	60.58	55.55	73.19	66.44	56.86
TESTES WITH EPIIDYMIDES (G)	5.661	5.681	5.639	5.071	5.509	5.503	5.146	5.382	5.710
% BRAIN WEIGHT	220.27	255.21	237.43	250.54	239.94	246.11	236.27	229.22	239.41

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THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 107
SEX: MALE

GROUP: 3-M - 1.5 mg base/kg/day
ALL FATES DAYS: 91-92 ALL BALANCES

ANIMAL ID: BALANCE NO.:	341	343	344	345	346	347	348	349	350
BODY WEIGHT (G)	553	533	592	587	598	506	602	609	512
ADRENAL GLANDS (G)	0.036	0.097	0.076	0.052	0.074	0.086	0.062	0.061	0.059
% BRAIN WEIGHT	1.48	4.23	3.18	2.32	3.14	4.00	2.75	2.77	2.70
BRAIN (G)	2.437	2.291	2.391	2.244	2.356	2.149	2.251	2.201	2.184
HEART (G)	1.753	1.672	1.914	1.887	2.009	2.287	1.832	2.183	1.661
% BRAIN WEIGHT	71.93	72.98	80.05	84.09	85.27	106.42	81.39	99.18	76.05
KIDNEYS (G)	4.812	4.568	4.952	5.100	5.119	3.630	4.916	5.277	4.559
% BRAIN WEIGHT	197.46	199.39	207.11	227.27	217.28	168.92	218.39	239.75	208.75
LIVER (G)	19.995	18.053	21.411	22.782	21.952	20.114	21.378	25.919	19.000
% BRAIN WEIGHT	820.48	788.00	895.48	1015.24	931.75	935.97	949.71	1177.60	869.96
SPLEEN (G)	1.942	1.651	1.839	1.810	2.052	1.604	2.079	1.769	1.747
% BRAIN WEIGHT	79.69	72.06	76.91	80.66	87.10	74.64	92.36	80.37	79.99
TESTES WITH EPIDIDYMIDES (G)	5.432	4.908	5.450	5.988	5.456	5.045	5.452	5.825	5.373
% BRAIN WEIGHT	222.90	214.23	227.94	266.84	231.58	234.76	242.20	264.65	246.02

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 107
SEX: MALE

GROUP: 4-M - 4.5 mg base/kg/day
ALL FATES DAYS: 91-92 ALL BALANCES

ANIMAL ID: BALANCE NO.:	362	364	365
BODY WEIGHT (G)	382	421	563
ADRENAL GLANDS (G)	0.061	0.055	0.073
% BRAIN WEIGHT	2.83	2.52	3.07
BRAIN (G)	2.157	2.185	2.381
HEART (G)	2.044	1.656	2.432
% BRAIN WEIGHT	94.76	75.79	102.14
KIDNEYS (G)	4.612	3.976	5.179
% BRAIN WEIGHT	213.82	181.97	217.51
LIVER (G)	22.954	18.657	25.636
% BRAIN WEIGHT	1064.16	853.87	1076.69
SPLEEN (G)	1.649	1.326	2.367
% BRAIN WEIGHT	76.45	60.69	99.41
TESTES WITH EPIDIDYMIDES (G)	4.234	4.962	6.100
% BRAIN WEIGHT	196.29	227.09	256.19

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 107
SEX: FEMALE

GROUP: 1-F - 0 mg base/kg/day
ALL FATES DAYS: 91-92 ALL BALANCES

ANIMAL ID: BALANCE NO.:	311	312	313	314	315	316	317	318	319
BODY WEIGHT (G)	320	335	368	297	300	315	334	305	323
ADRENAL GLANDS (G)	0.103	0.069	0.078	0.086	0.124	0.097	0.113	0.114	0.082
% BRAIN WEIGHT	4.70	3.09	3.53	4.30	6.49	4.92	5.31	5.57	3.77
BRAIN (G)	2.190	2.232	2.207	2.001	1.910	1.973	2.128	2.048	2.176
HEART (G)	1.454	1.292	1.329	1.020	1.288	1.132	1.361	0.986	1.130
% BRAIN WEIGHT	66.39	57.89	60.22	50.97	67.43	57.37	63.96	48.14	51.93
KIDNEYS (G)	2.928	2.684	2.544	2.555	2.450	2.661	2.836	2.437	2.534
% BRAIN WEIGHT	133.70	120.25	115.27	127.69	128.27	134.87	133.27	118.99	116.45
LIVER (G)	13.910	11.910	14.792	10.640	11.105	10.856	12.299	11.348	11.142
% BRAIN WEIGHT	635.16	533.60	670.23	531.73	581.41	550.23	577.96	554.10	512.04
OVARIES (G)	0.180	0.154	0.099	0.162	0.114	0.136	0.232	0.226	0.202
% BRAIN WEIGHT	8.22	6.90	4.49	8.10	5.97	6.89	10.90	11.04	9.28
SPLEEN (G)	0.635	0.706	0.717	0.549	0.628	0.698	0.814	0.917	0.704
% BRAIN WEIGHT	29.00	31.63	32.49	27.44	32.88	35.38	38.25	44.78	32.35

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 107
SEX: FEMALE

GROUP: 1-F - 0 mg base/kg/day
ALL FATES DAYS: 91-92 ALL BALANCES

ANIMAL ID: 320
BALANCE NO.:

BODY WEIGHT (G) 317

ADRENAL GLANDS (G) 0.084
% BRAIN WEIGHT 4.03

BRAIN (G) 2.086

HEART (G) 1.625
% BRAIN WEIGHT 77.90

KIDNEYS (G) 2.782
% BRAIN WEIGHT 133.37

LIVER (G) 12.678
% BRAIN WEIGHT 607.77

OVARIES (G) 0.205
% BRAIN WEIGHT 9.83

SPLEEN (G) 0.978
% BRAIN WEIGHT 46.88

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THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 107
SEX: FEMALE

GROUP: 2-F - 0.5 mg base/kg/day
ALL FATES DAYS: 91-92 ALL BALANCES

ANIMAL ID: BALANCE NO.:	331	332	333	334	335	336	337	338	339
BODY WEIGHT (G)	437	281	378	344	339	374	317	318	274
ADRENAL GLANDS (G)	0.134	0.097	0.089	0.104	0.083	0.085	0.079	0.067	0.079
% BRAIN WEIGHT	6.51	4.66	4.39	4.97	3.69	4.46	3.71	3.12	4.03
BRAIN (G)	2.057	2.082	2.029	2.093	2.251	1.907	2.129	2.147	1.961
HEART (G)	1.360	1.118	1.481	1.161	1.273	1.378	1.257	1.440	1.303
% BRAIN WEIGHT	66.12	53.70	72.99	55.47	56.55	72.26	59.04	67.07	66.45
KIDNEYS (G)	3.221	2.507	2.624	2.606	2.754	2.706	2.649	2.632	2.502
% BRAIN WEIGHT	156.59	120.41	129.32	124.51	122.35	141.90	124.42	122.59	127.59
LIVER (G)	13.929	9.953	12.955	10.926	11.413	13.899	11.182	13.898	9.193
% BRAIN WEIGHT	677.15	478.05	638.49	522.03	507.02	728.84	525.22	647.32	468.79
OVARIES (G)	0.152	0.112	0.220	0.110	0.170	0.164	0.138	0.178	0.076
% BRAIN WEIGHT	7.39	5.38	10.84	5.26	7.55	8.60	6.48	8.29	3.88
SPLEEN (G)	1.021	0.651	0.921	0.875	0.758	0.778	0.659	0.821	0.468
% BRAIN WEIGHT	49.64	31.27	45.39	41.81	33.67	40.80	30.95	38.24	23.87

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 107
SEX: FEMALE

GROUP: 2-F - 0.5 mg base/kg/day
ALL FATES DAYS: 91-92 ALL BALANCES

ANIMAL ID: 340
BALANCE NO.:

BODY WEIGHT (G)	323
ADRENAL GLANDS (G)	0.120
% BRAIN WEIGHT	5.28
BRAIN (G)	2.274
HEART (G)	1.149
% BRAIN WEIGHT	50.53
KIDNEYS (G)	2.773
% BRAIN WEIGHT	121.94
LIVER (G)	11.876
% BRAIN WEIGHT	522.25
OVARIES (G)	0.134
% BRAIN WEIGHT	5.89
SPLEEN (G)	0.659
% BRAIN WEIGHT	28.98

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 107
SEX: FEMALE

GROUP: 3-F - 1.5 mg base/kg/day
ALL FATES DAYS: 91-92 ALL BALANCES

ANIMAL ID: BALANCE NO.:	351	352	353	354	355	356	357	358	359
BODY WEIGHT (G)	292	328	374	331	380	342	321	306	268
ADRENAL GLANDS (G)	0.091	0.088	0.077	0.109	0.033	0.085	0.135	0.084	0.064
% BRAIN WEIGHT	4.39	4.40	3.77	5.16	1.67	4.05	7.15	4.11	3.05
BRAIN (G)	2.073	2.002	2.040	2.111	1.981	2.097	1.887	2.046	2.098
HEART (G)	1.119	1.191	1.318	1.268	1.295	1.148	1.247	1.596	1.258
% BRAIN WEIGHT	53.98	59.49	64.61	60.07	65.37	54.74	66.08	78.01	59.96
KIDNEYS (G)	2.691	2.783	2.741	3.352	2.774	3.144	2.778	2.515	2.716
% BRAIN WEIGHT	129.81	139.01	134.36	158.79	140.03	149.93	147.22	122.92	129.46
LIVER (G)	9.532	12.838	12.576	13.183	11.778	13.889	13.557	14.308	11.138
% BRAIN WEIGHT	459.82	641.26	616.47	624.49	594.55	662.33	718.44	699.32	530.89
OVARIES (G)	0.130	0.130	0.107	0.114	0.168	0.144	0.245	0.091	0.091
% BRAIN WEIGHT	6.27	6.49	5.25	5.40	8.48	6.87	12.98	4.45	4.34
SPLEEN (G)	1.008	1.081	0.960	1.199	1.083	1.010	0.973	1.011	0.613
% BRAIN WEIGHT	48.63	54.00	47.06	56.80	54.67	48.16	51.56	49.41	29.22

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 107
SEX: FEMALE

GROUP: 3-F - 1.5 mg base/kg/day
ALL FATES DAYS: 91-92 ALL BALANCES

ANIMAL ID: 360
BALANCE NO.:

BODY WEIGHT (G) 395

ADRENAL GLANDS (G) 0.078
% BRAIN WEIGHT 3.58

BRAIN (G) 2.179

HEART (G) 1.322
% BRAIN WEIGHT 60.67

KIDNEYS (G) 3.184
% BRAIN WEIGHT 146.12

LIVER (G) 12.451
% BRAIN WEIGHT 571.41

OVARIES (G) 0.102
% BRAIN WEIGHT 4.68

SPLEEN (G) 0.910
% BRAIN WEIGHT 41.76

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 107
SEX: FEMALE

GROUP: 4-F - 4.5 mg base/kg/day
ALL FATES DAYS: 91-92 ALL BALANCES

ANIMAL ID: BALANCE NO.:	371	372	373	374	375	376	377	378	379
BODY WEIGHT (G)	357	307	319	295	340	237	289	288	320
ADRENAL GLANDS (G)	0.109	0.086	0.065	0.083	0.085	0.064	0.095	0.098	0.096
% BRAIN WEIGHT	5.00	4.01	3.32	4.41	3.93	3.14	4.82	4.44	4.94
BRAIN (G)	2.179	2.146	1.958	1.880	2.163	2.037	1.972	2.207	1.945
HEART (G)	1.243	1.328	1.099	1.188	1.374	0.881	1.309	1.098	1.233
% BRAIN WEIGHT	57.04	61.88	56.13	63.19	63.52	43.25	66.38	49.75	63.39
KIDNEYS (G)	3.377	2.999	3.080	2.720	3.431	2.190	2.792	2.864	3.477
% BRAIN WEIGHT	154.98	139.75	157.30	144.68	158.62	107.51	141.58	129.77	178.77
LIVER (G)	16.012	12.879	11.811	12.541	13.873	10.639	12.309	11.799	13.488
% BRAIN WEIGHT	734.83	600.14	603.22	667.07	641.38	522.29	624.19	534.62	693.47
OVARIES (G)	0.223	0.151	0.088	0.191	0.195	0.154	0.114	0.109	0.120
% BRAIN WEIGHT	10.23	7.04	4.49	10.16	9.02	7.56	5.78	4.94	6.17
SPLEEN (G)	1.827	1.552	1.327	1.690	1.843	1.439	1.756	1.283	1.603
% BRAIN WEIGHT	83.85	72.32	67.77	89.89	85.21	70.64	89.05	58.13	82.42

THIRTEEN WEEK ORAL TOXICITY
STUDY OF WR242511 IN RATS

INDIVIDUAL ORGAN WEIGHTS

STUDY: 107
SEX: FEMALE

GROUP: 4-F - 4.5 mg base/kg/day
ALL FATES DAYS: 91-92 ALL BALANCES

ANIMAL ID: 380
BALANCE NO.:

BODY WEIGHT (G) 297

ADRENAL GLANDS (G) 0.091
% BRAIN WEIGHT 4.64

BRAIN (G) 1.963

HEART (G) 1.231
% BRAIN WEIGHT 62.71

KIDNEYS (G) 2.897
% BRAIN WEIGHT 147.58

LIVER (G) 12.541
% BRAIN WEIGHT 638.87

OVARIES (G) 0.193
% BRAIN WEIGHT 9.83

SPLEEN (G) 1.466
% BRAIN WEIGHT 74.68

DRAFT

APPENDIX 10
Pathology Report

DRAFT PATHOLOGY REPORT FOR
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TRL STUDY NUMBER 107

PREPARED
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SEPTEMBER 26, 1994

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SECTION I
PATHOLOGY NARRATIVE

DRAFT PATHOLOGY REPORT

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS

INTRODUCTION

This pathology report, submitted by Pathology Associates, Inc. (PAI) to Toxicology Research Laboratory (TRL), University of Illinois at Chicago, represents the pathology findings for the study designated as "Thirteen Week Oral Toxicity Study of WR242511 in Rats", TRL Study Number 107.

EXPERIMENTAL DESIGN AND METHODS

Three groups, each composed of 10 male and 10 female Virus Antibody Free CD® rats, were given the test article, WR242511, once daily by gavage, starting with Day 0, for at least 13 weeks. Dose levels of the test article were 0.5, 1.5, and 4.5 mg base/kg/day (mbkd), as indicated in the Summary of Experimental Design (see Table I). A fourth group of 10 male and 10 female rats received the vehicle (1% methylcellulose/0.2% Tween 80) on the same schedule. Dosing volume was 5 ml/kg in all groups. Nine animals, all males, died or were sacrificed moribund during the study (early deaths). Treatment group, week of death, disposition, and histopathologic lesions that contributed to the death of these animals are given in Table III, Summary of Early Deaths. Animals that survived until the scheduled termination of the study were sacrificed and necropsied in random order on Days 91 and 92. Necropsies of all animals were conducted according to TRL Standard Operating Procedures. Tissues required by the protocol (see Table II, Protocol-Required Tissues) were examined and placed in 10% neutral buffered formalin. Tissues required for histopathologic evaluation in vehicle control and high dose (4.5 mbkd) groups and the one middle (1.5 mbkd) dose animal which was found dead during the study were trimmed, processed, and slides were prepared in accordance with PAI Standard Operating Procedures. Tissues were then evaluated by light microscopy and results were tabulated. Thymus, liver, and lung in males, and spleen and lung in females were identified as potential target tissues. These tissues in the low (0.5 mbkd) and middle (1.5 mbkd) dose groups were then similarly processed and evaluated.

Microscopic findings for all groups are summarized in the Project Summary Tables (Section II). The mean group severity scores are found in the Severity Summary Tables (Section III). The mean group severity scores were determined by dividing the sum of all severity scores for a finding by the number of tissues examined. Microscopic findings in the protocol-required tissues for individual animals are presented in the Tabulated Animal Data Tables (Section IV). The correlation of the necropsy findings and histopathology findings are reported in the Correlation of Gross and Microscopic (Micro) Findings (Section V). The codes used as entries in these tables are explained in the Report Codes Table. Abbreviations used in these tables are explained in the Abbreviation List.

RESULTS AND DISCUSSION

The Results and Discussion section is divided into three parts: Necropsy Findings, Diagnostic Terms, and Histopathology Findings. The Necropsy Findings portion gives lesions seen at necropsy that were test article-related. The Diagnostic Terms portion lists and clarifies diagnostic

terminology that may be unclear. Terms listed in the Diagnostic Terms portion of this section were not necessarily considered to be test article-related. The Histopathology Findings portion of this section reports the results and provides discussion of the histopathologic evaluation of the tissues.

Necropsy Findings

Potentially test article-related lesions were seen at necropsy in the liver of males and in the lung of males and females. The liver lesions occurred only in males in the 4.5 mbkd dose group that died or were sacrificed moribund prior to the scheduled terminal sacrifice. These were variably described as mottled lesion; pale, diffuse lesion; irregular, linear pigmentation; or irregular, diffuse, dark lesion, and occurred in 6 out of the 7 early deaths in this group of males. No potentially test article-related lesions were seen in the livers of males that were sacrificed at the scheduled terminal sacrifice.

In the lungs, potentially test article-related lesions were seen at necropsy in 5 out of 10 and 3 out of 10 males in the 1.5 and 4.5 mbkd dose groups, respectively. The 3 males in the 4.5 mbkd dose group that had lesions in the lung at necropsy had all survived until the terminal sacrifice. The 7 males in this group that were early deaths did not have lesions in the lungs at necropsy. In females, similar lung lesions were observed at necropsy in 8 out of 10 and 10 out of 10 animals in the 1.5 and 4.5 mbkd dose groups, respectively. These lesions were bilateral, multiple, irregular, linear, and white.

Diagnostic Terms

The morphologic characteristics of observations and lesions which require comment are presented in subsequent paragraphs to aid in the interpretation of the data.

Liver

Hepatocyte degeneration, when present, tended to occur throughout the liver. Affected hepatocytes were swollen, resulting in obstruction of adjacent bile canaliculi. The cytoplasm in most hepatocytes was pale with a ground-glass appearance but vacuolated in some cells. In some animals, there was an increase in nuclei in periportal zones that suggested oval cell proliferation. Unequivocal oval cell proliferation could not be identified, though. Hepatocyte necrosis occurred in randomly scattered individual hepatocytes. These cells had undergone coagulative necrosis and had pyknotic or karyorrhectic nuclei.

Lung

Alveolar histiocytosis occurred throughout the lung. Large macrophages containing abundant, finely vacuolated, pale cytoplasm were found individually or in small numbers in alveoli or clustered in large numbers in alveoli surrounding terminal bronchioles. Perivascular infiltrates of macrophages and lymphocytes occurred in association with alveolar histiocytosis. Heterophils were rare, and there was no proteinic exudate.

Spleen

Hemosiderin pigment in the spleen was represented by golden-brown granular pigment filling the cytoplasm of macrophages in the sinusoids.

Thymus

Lymphocyte depletion was diagnosed in the thymus when thymic lymphocytes were decreased in number. This occurred in cortical and medullary zones.

The remainder of the diagnoses used in this study were considered to be self-explanatory and were not discussed in this section.

Histopathology Findings

Liver

Hepatocyte degeneration was diagnosed in 0 out of 10, 0 out of 10, 4 out of 10, and 10 out of 10 males in the vehicle control, 0.5, 1.5, and 4.5 mbkd dose groups, with mean group severity scores of 0.00, 0.00, 0.40, and 2.70, respectively. Hepatocyte necrosis was diagnosed in 0 out of 10, 0 out of 10, 1 out of 10, and 10 out of 10 males in the vehicle control, 0.5, 1.5, and 4.5 mbkd dose groups, with mean group severity scores of 0.00, 0.00, 0.10, and 1.70, respectively. Neither hepatocyte degeneration nor hepatocyte necrosis was diagnosed in females. Both incidence and mean group severity scores for hepatocyte degeneration and hepatocyte necrosis in males were dose-related. The initial response of hepatocytes to toxic injury is acute cell swelling due to loss of the cell's ability to regulate water flux. Acute cell swelling in hepatocytes results in a ground-glass to vacuolated character in the cytoplasm such as seen in degenerate hepatocytes in these animals. Cells which have been injured and undergone acute cell swelling may either recover or undergo necrosis.¹ Necrosis of scattered hepatocytes such as seen in males in the 1.5 and 4.5 mbkd dose groups in this study is consistent with xenobiotic associated hepatocyte necrosis.² For these reasons, and because of the dose response of incidence and mean group severity scores, hepatocyte degeneration and hepatocyte necrosis were interpreted as test article-related changes in males. These histopathologic changes correlated to the lesions seen at necropsy in the livers of males in the 4.5 mbkd dose group.

Focal necrosis occurred in the liver of one male and two females in the vehicle control group. Focal necrosis is a commonly observed change in animals and has been associated with infections, parasite migration, and biliary obstruction.³ As it occurred only in vehicle control animals, focal necrosis was considered not to be related to the test article. It should not be confused with the hepatocyte necrosis that was a test article-related change in males.

Lung

Alveolar histiocytosis was diagnosed in 1 out of 10, 4 out of 10, 8 out of 10, and 10 out of 10 males in the vehicle control, 0.5, 1.5, and 4.5 mbkd dose groups, with mean group severity scores of 0.10, 0.40, 1.40, and 1.50, respectively. In females, this change occurred in 0 out of 10, 1 out of 10, 9 out of 10, and 10 out of 10 animals in the vehicle control, 0.5, 1.5, and 4.5 mbkd dose groups, with mean group severity scores of 0.00, 0.10, 1.40, and 2.00, respectively. These incidence and mean group severity scores were interpreted as dose related. The macrophages in alveolar histiocytosis in treated animals in this study were morphologically similar to those that occur in spontaneous alveolar histiocytosis. Spontaneous alveolar histiocytosis differs from the alveolar histiocytosis described above in that it is usually seen in older animals and occurs as single foci located subpleurally or in the periphery of the lung. The alveolar histiocytosis which occurred in 1 out of 10 vehicle control males was consistent with spontaneous alveolar histiocytosis.

Non-cytotoxic materials that reach the alveolar zone of the lung will be cleared by the mucociliary system and phagocytosis by macrophages.⁴ Macrophages with a similar appearance can infiltrate the parenchyma of the lung in order to clear proteins that may have leaked into alveoli due to injury to the pulmonary microvascular bed.⁵ Proteinic material, including fibrinogen, fibrin, or other proteins, was not seen in the lung of treated animals in this study, but the perivascular cellular infiltrates that occurred in association with alveolar

histiocytosis do suggest vascular injury. The severity of the injury was most likely mild such that the rate of release of proteins into the alveoli did not exceed the rate at which the macrophages were able to clear them. For these reasons, alveolar histiocytosis was interpreted as a test article-related change in males and in females. As animals in the 0.5 mbkd dose group were affected, a no-effect level for alveolar histiocytosis was not determined. The multiple, irregular, linear, white lesions seen at necropsy in the lungs of males and females in the 1.5 and 4.5 mbkd dose groups correlated with alveolar histiocytosis.

Spleen

Increased hemosiderin pigment was diagnosed in 9 out of 10 females in the 4.5 mbkd dose group with a mean group severity score of 1.20. This change did not occur in females in the vehicle control, 0.5, or 1.5 mbkd dose groups. In males, increased splenic hemosiderin was not diagnosed in the 4.5 mbkd or vehicle control dose groups, but did occur in the one male in the 1.5 mbkd dose group in which the spleen was evaluated. Excess iron in the body, such as that released from erythrocytes by hemolysis or hemorrhage into body tissues, is normally stored as hemosiderin in the liver, spleen, and bone marrow. These deposits are visible by light microscopy, especially in the rat spleen. This hemosiderin is readily available for use in erythropoiesis, which also normally occurs in the spleen of adult rats. Hemosiderin deposits which are increased due to an episode of hemorrhage or hemolysis will be gradually depleted over time. The rate of depletion will be dependent on the amount of hemosiderin deposited and the rate at which erythropoiesis proceeds. In this study, increased hemosiderin pigment in the spleen occurred in females in the highest dose group (4.5 mbkd). This observation is consistent with the splenic hemosiderin deposits being due to mild hemolytic anemia which did not result in a detectable test article-related increase in hematopoiesis. For these reasons, increased splenic hemosiderin deposition was interpreted as a test article-related change in females. It was considered to be most likely secondary to mild hemolytic anemia. As splenic hemosiderin deposition did not occur in males in the 4.5 mbkd dose group, the occurrence of this change in one male in the 1.5 mbkd dose group was considered most likely an incidental finding.

Thymus

Thymic lymphocyte depletion was diagnosed in 0 out of 10, 0 out of 10, 1 out of 10, and 4 out of 7 males in the vehicle control, 0.5, 1.5, and 4.5 mbkd dose groups, with mean group severity scores of 0.00, 0.00, 0.40, and 1.57, respectively. Thymic lymphocyte depletion was not diagnosed in females. All three males in the 4.5 mbkd dose group that had no thymus available for microscopic evaluation were found dead or sacrificed moribund (#366, #367, and #368). All three of these animals had hepatocyte degeneration and necrosis in the liver and alveolar histiocytosis in the lung to the extent that these lesions were the probable cause of death or moribund condition for these animals. These observations suggest that the thymus in these animals was too small to be identified at fixed tissue trimming. The four animals in the 4.5 mbkd dose group that had thymic lymphocyte depletion also had hepatocyte degeneration and necrosis in the liver and alveolar histiocytosis in the lung. Of these four animals, two were sacrificed moribund (#361 and #370), one was found dead (#363), and one was sacrificed at the termination of the study (#362). Animal #342 in the 1.5 mbkd dose group had severe thymic lymphocyte depletion and mild alveolar histiocytosis but no lesions suggestive of hepatotoxicity. The probable cause of death in this animal was severe chronic-active inflammation involving the heart, pleura of the lung, and diaphragm.

Thymic lymphocytes are highly susceptible to the effects of toxic compounds, glucocorticoid hormones, and radiation. With respect to glucocorticoids, thymic lymphocyte depletion occurs in response to either endogenous (so called stress hormones) or exogenous glucocorticoids.⁶ Depletion of thymic lymphocytes at low incidence and severity in subchronic toxicity studies is

commonly attributed to endogenous glucocorticoid release (stress). Thymic lymphocyte depletion in animal #342 in the 1.5 mbkd dose group was attributed to stress caused by the severe and diffuse chronic-active inflammation that occurred in the heart, pleura of the lung, and diaphragm. All four of the males in the 4.5 mbkd dose group that had thymic lymphocyte depletion also had test article-related toxicity in the liver and lung. Three of these four animals were sacrificed moribund (#361 and #370) or died prior to the end of the study (#363). The cause of moribund condition or death for all three of these animals was test article-related liver and lung toxicity. For these reasons, thymic lymphocyte depletion was interpreted as a test article-related change in males. It is not clear, however, whether this change was due to generalized stress or to a direct effect of the test article.

Other Lesions

Several other lesions occurred in other tissues examined in this study. Among these lesions were cellular infiltrates and chronic inflammation in the harderian gland. These changes occurred in vehicle control and 4.5 mbkd dose groups and were attributed to orbital sinus blood collection. No source of the hemorrhage seen in the lung of animal #328 (0.5 mbkd, accidental death) was identified. The diffuse distribution of the hemorrhage suggests that the blood was inhaled into the lungs and caused death by asphyxiation. All other lesions were considered incidental and not to warrant further discussion.

CONCLUSIONS

Under the conditions of this study, administration of WR242511 to rats by gavage for thirteen weeks was associated with hepatocyte degeneration, hepatocyte necrosis, and thymic lymphocyte depletion in males. These effects occurred in the 1.5 and 4.5 mbkd dose groups in a dose-related manner. Splenic hemosiderin deposition in females was considered to be secondary to test article-related hemolytic anemia and not a direct effect of the test article. Alveolar histiocytosis in the lung was a test article-related change which occurred in the lung of both males and females in all groups given the test article, indicating that a no-effect level was not determined.

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Date

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TABLE I

SUMMARY OF EXPERIMENTAL DESIGN

Treatment Group	Treatment	Dose Level (mg base/kg/day)	Number of Animals	
			Males	Females
1	Vehicle	0	10	10
2	WR242511	0.5	10	10
3	WR242511	1.5	10	10
4	WR242511	4.5	10	10

TABLE II

PROTOCOL-REQUIRED TISSUES

Adrenal glands	Pituitary
Aorta	Prostate
Brain (fore-, mid-, and hind-)	Rectum
Cecum	Salivary gland (submaxillary)
Colon	Sciatic nerve
Diaphragm	Seminal vesicles
Duodenum	Skeletal muscle
Esophagus	Skin/Mammary gland
Eyes with Harderian gland	Spinal cord (thoracic)
Femur with marrow	Spleen
Gross lesions	Stomach
Heart	Testes/Epididymides
Ileum	Thymus
Jejunum	Thyroid glands/Parathyroids
Kidneys	Tongue
Liver	Trachea
Lungs/Bronchi	Urinary bladder
Lymph node (mesenteric)	Uterus
Ovaries	Vagina
Pancreas	

TABLE III

SUMMARY OF EARLY DEATHS^A

TREATMENT GROUP	ANIMAL NUMBER	WEEKS ON STUDY	DISPOSITION	HISTOPATHOLOGIC LESIONS CONTRIBUTING TO DEATH OR MORIBUND CONDITION
0.5 mbkd	328	13	Accidental Death	Lung: Hemorrhage
1.5 mbkd	342	13	Found Dead	Chronic Active Inflammation involving heart and lung (pleura), probably secondary to esophageal injury Thymus: Depletion, lymphocyte
4.5 mbkd	361	5	Moribund Sacrifice	Liver: Hepatocyte degeneration and necrosis Lung: Alveolar histiocytosis Thymus: Depletion, lymphocyte
4.5 mbkd	363	4	Found Dead	Liver: Hepatocyte degeneration and necrosis Lung: Alveolar histiocytosis Thymus: Depletion, lymphocyte
4.5 mbkd	366	4	Found Dead	Liver: Hepatocyte degeneration and necrosis Lung: Alveolar histiocytosis
4.5 mbkd	367	10	Moribund Sacrifice	Liver: Hepatocyte degeneration and necrosis Lung: Alveolar histiocytosis
4.5 mbkd	368	4	Moribund Sacrifice	Liver: Hepatocyte degeneration and necrosis Lung: Alveolar histiocytosis
4.5 mbkd	369	3	Moribund Sacrifice	Liver: Hepatocyte degeneration and necrosis Lung: Alveolar histiocytosis
4.5 mbkd	370	5	Moribund Sacrifice	Liver: Hepatocyte degeneration and necrosis Lung: Alveolar histiocytosis Thymus: Depletion, lymphocyte

A: All early death animals were males.

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Report Codes Table

D R A F T

A. Codes applying to organs

N	Tissues within normal histological limits
A	Autolysis precluding adequate evaluation
P	Paired organ missing
U	Tissues unsuitable for complete evaluation
S	Tissues not applicable to animal
*	Tissues not required by protocol

B. Codes applying to microscopic diagnoses

1	minimal
2	mild
3	moderate
4	marked
)	focal
]	locally extensive
>	multifocal
P	Present
B	Neoplasm, benign
M	Neoplasm, malignant without metastasis
C	Neoplasm, malignant with metastasis
X	Metastatic site (+)
-	No data entered

HISTOPATHOLOGY TABLES

ABBREVIATION LIST

basophil - basophilia

bd - body

chr-act - chronic-active

epith - epithelium

fr - foreign

inflam - inflammation

mbkd - mg base/kg/day

mus - muscle

myocard - myocardium

NOS - not otherwise specified

pericard - pericardium

regenerat - regeneration

skl - skeletal

Veh Con - vehicle control

vnt - ventral

SECTION II
PROJECT SUMMARY TABLE

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Project Summary Table

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

D R A F T

PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

PAGE 15

WEEKS: 3-14

SEX: MALE

GROUP:

NUMBER OF ANIMALS:

Veh Con
10

0.5mbkd
10

1.5mbkd
10

4.5mbkd
10

	#	%	#	%	#	%	#	%
TRACHEA	# Ex 10		0		1		10	
AORTA	# Ex 10		0		1		10	
COLON	# Ex 10		0		1		10	
DUODENUM	# Ex 10		0		0		8	
HEART	# Ex 10		0		1		10	
Cardiomyopathy	9	(90)	0		0	(0)	3	(30)
Inflammation, subacute	0	(0)	0		0	(0)	1	(10)
Myocard, inflam, chr-act	0	(0)	0		1	(100)	0	(0)
Pericard, inflam, chr-act	0	(0)	0		1	(100)	0	(0)
STOMACH	# Ex 10		0		1		10	
Forestomach, inflam, acute	0	(0)	0		0	(0)	1	(10)
JEJUNUM	# Ex 10		0		0		8	
LIVER	# Ex 10		10		10		10	
Bile duct, hyperplasia	0	(0)	0	(0)	0	(0)	1	(10)
Hepatocyte, degeneration	0	(0)	0	(0)	4	(40)	10	(100)
Hepatocyte, necrosis	0	(0)	0	(0)	1	(10)	10	(100)
Infiltrate, cellular	1	(10)	2	(20)	0	(0)	0	(0)
Necrosis, focal	1	(10)	0	(0)	0	(0)	0	(0)
SPLEEN	# Ex 10		0		1		10	
Depletion, lymphocyte	0	(0)	0		0	(0)	1	(10)
Pigment, hemosiderin	0	(0)	0		1	(100)	0	(0)

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D R A F T

PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

PAGE 16

WEEKS: 3-14

SEX: MALE

GROUP:

NUMBER OF ANIMALS:

Veh Con
10

0.5mbkd
10

1.5mbkd
10

4.5mbkd
10

	#	%	#	%	#	%	#	%
LUNG	# Ex	10	10	10	10	10		
Alveolar histiocytosis		1 (10)	4 (40)	8 (80)	10 (100)			
Congestion		0 (0)	0 (0)	1 (10)	1 (10)			
Hemorrhage		1 (10)	4 (40)	3 (30)	0 (0)			
Inflammation, subacute		7 (70)	3 (30)	2 (20)	0 (0)			
Pleura, inflam, chr-act		0 (0)	0 (0)	1 (10)	0 (0)			
Pleura, inflam, chronic, fr bd		0 (0)	1 (10)	0 (0)	0 (0)			
KIDNEY	# Ex	10	0	1	10			
Nephropathy		0 (0)	0	0 (0)	3 (30)			
Renal tubule, casts, proteinic		1 (10)	0	0 (0)	0 (0)			
Renal tubule, dilatation		2 (20)	0	0 (0)	0 (0)			
Renal tubule, epith, basophil		1 (10)	0	0 (0)	0 (0)			
Renal tubule, epith, regenerat		1 (10)	0	0 (0)	0 (0)			
LYMPH NODE, MESENTERIC	# Ex	10	0	1	10			
URINARY BLADDER	# Ex	10	0	1	10			
Calculus		1 (10)	0	0 (0)	2 (20)			
Mucosa, inflammation, acute		0 (0)	0	0 (0)	2 (20)			
Mucosa, ulcer		0 (0)	0	0 (0)	1 (10)			
PROSTATE	# Ex	10	0	1	10			
Infiltrate, cellular		1 (10)	0	0 (0)	1 (10)			
SKIN	# Ex	10	0	1	10			
MAMMARY GLAND	# Ex	10	0	0	10			
Atrophy		0 (0)	0	0	2 (20)			
CECUM	# Ex	10	0	0	9			

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D R A F T

PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

PAGE 17

WEEKS: 3-14

SEX: MALE

GROUP:

NUMBER OF ANIMALS:

Veh Con

10

0.5mbkd

10

1.5mbkd

10

4.5mbkd

10

	#	%	#	%	#	%	#	%
ILEUM	# Ex 10		0		0		9	
RECTUM	# Ex 10		0		0		10	
SCIATIC NERVE	# Ex 10		0		0		7	
SKELETAL MUSCLE	# Ex 10		0		1		10	
EPIDIDYMIS	# Ex 10		0		1		10	
Granuloma, sperm	0	(0)	0		0	(0)	1	(10)
Hypospermia	0	(0)	0		0	(0)	1	(10)
SEMINAL VESICLE	# Ex 10		0		1		10	
TESTIS	# Ex 10		0		1		10	
Atrophy	0	(0)	0		0	(0)	1	(10)
DIAPHRAGM	# Ex 10		0		1		9	
Inflammation, chronic-active	0	(0)	0		1	(100)	0	(0)
TONGUE	# Ex 10		0		1		10	
FEMUR	# Ex 10		0		1		10	
BONE MARROW	# Ex 10		0		1		10	
Hyperplasia, myeloid	0	(0)	0		1	(100)	0	(0)

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PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Project Summary Table

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

DRAFT

PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

PAGE 18

WEEKS: 3-14

SEX: MALE

GROUP:

NUMBER OF ANIMALS:

Veh Con
10

0.5mbkd
10

1.5mbkd
10

4.5mbkd
10

	#	%	#	%	#	%	#	%
EYE	# Ex	10	0	0	0	9		
HARDERIAN GLAND	# Ex	10	0	1	10			
Infiltrate, cellular		5 (50)	0	0 (0)	1 (10)			
Inflammation, chronic		1 (10)	0	0 (0)	0 (0)			

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PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Project Summary Table

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DRAFT

PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

PAGE 19

WEEKS: 3-14

SEX: MALE

GROUP:

Veh Con

0.5mbkd

1.5mbkd

4.5mbkd

NUMBER OF ANIMALS:

10

10

10

10

OTHER TISSUES AND LESIONS:

% # % # % # %

SKL MUS, VNT - Inflam, chr-act

0 (0)

0 (0)

1 (10)

0 (0)

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PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Project Summary Table

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D R A F T

PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

PAGE 20

WEEKS: 3-14

SEX: FEMALE

GROUP:

NUMBER OF ANIMALS:

Veh Con
10

0.5mbkd
10

1.5mbkd
10

4.5mbkd
10

	#	%	#	%	#	%	#	%
BRAIN	# Ex	10	0	0	0	10		
Lateral ventricle, hemorrhage	1	(10)	0	0	0	0	(0)	
PITUITARY GLAND	# Ex	10	0	0	0	10		
Pars distalis, cyst	1	(10)	0	0	0	3	(30)	
SPINAL CORD, THORACIC	# Ex	10	0	0	0	10		
PANCREAS	# Ex	10	0	0	0	10		
SALIVARY GLAND	# Ex	10	0	0	0	10		
THYMUS	# Ex	10	0	0	0	10		
ADRENAL GLAND	# Ex	10	0	0	0	10		
Cortex, vacuolation, cytoplasm	0	(0)	0	0	0	1	(10)	
ESOPHAGUS	# Ex	10	0	0	0	10		
PARATHYROID GLAND	# Ex	10	0	0	0	8		
THYROID GLAND	# Ex	10	0	0	0	10		
TRACHEA	# Ex	10	0	0	0	10		
Infiltrate, cellular	0	(0)	0	0	0	1	(10)	
AORTA	# Ex	10	0	0	0	10		

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Project Summary Table

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D R A F T

PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

PAGE 21

WEEKS: 3-14

SEX: FEMALE

GROUP:

NUMBER OF ANIMALS:

Veh Con
10

0.5mbkd
10

1.5mbkd
10

4.5mbkd
10

		#	%	#	%	#	%	#	%
COLON	# Ex	10		0		0		10	
DUODENUM	# Ex	10		0		0		10	
HEART	# Ex	10		0		0		10	
Cardiomyopathy		3	(30)	0		0		3	(30)
STOMACH	# Ex	10		0		0		10	
JEJUNUM	# Ex	10		0		0		10	
LIVER	# Ex	10		0		0		10	
Necrosis, focal		2	(20)	0		0		0	(0)
SPLEEN	# Ex	10		10		10		10	
Extramedullary hematopoiesis		0	(0)	0	(0)	0	(0)	1	(10)
Pigment, hemosiderin		0	(0)	0	(0)	0	(0)	9	(90)
LUNG	# Ex	10		10		10		10	
Alveolar histiocytosis		0	(0)	1	(10)	9	(90)	10	(100)
Hemorrhage		2	(20)	2	(20)	1	(10)	0	(0)
Inflammation, subacute		2	(20)	0	(0)	1	(10)	0	(0)
KIDNEY	# Ex	10		0		0		10	
Cortex, fibrosis		1	(10)	0		0		0	(0)
Nephrocalcinosis		9	(90)	0		0		6	(60)
Renal tubule, casts, proteinic		0	(0)	0		0		1	(10)
Renal tubule, dilatation		1	(10)	0		0		0	(0)

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PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Project Summary Table

SUMMARY: Incidence of NEOPLASTIC and NON-NEOPLASTIC Microscopic Findings

DRAFT

PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

PAGE 22

WEEKS: 3-14

SEX: FEMALE

GROUP:

Veh Con

0.5mbkd

1.5mbkd

4.5mbkd

NUMBER OF ANIMALS:

10

10

10

10

	#	%	#	%	#	%	#	%
LYMPH NODE, MESENTERIC	# Ex 10		0		0		10	
URINARY BLADDER	# Ex 10		0		0		10	
SKIN	# Ex 10		0		0		10	
MAMMARY GLAND	# Ex 10		0		0		10	
CECUM	# Ex 10		0		0		10	
ILEUM	# Ex 10		0		0		10	
RECTUM	# Ex 10		0		0		10	
SCIATIC NERVE	# Ex 10		0		0		10	
SKELETAL MUSCLE	# Ex 10		0		0		10	
OVARY	# Ex 10		0		0		10	
UTERUS	# Ex 10		0		0		10	
Dilatation	1 (10)		0		0		3 (30)	
VAGINA	# Ex 9		0		0		10	
DIAPHRAGM	# Ex 10		0		0		10	

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PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
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PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

PAGE 23

WEEKS: 3-14

SEX: FEMALE

GROUP:

NUMBER OF ANIMALS:

Veh Con
10

0.5mbkd
10

1.5mbkd
10

4.5mbkd
10

	#	%	#	%	#	%	#	%
TONGUE	# Ex	10	0	0	0	10		
FEMUR	# Ex	10	0	0	9			
BONE MARROW	# Ex	10	0	0	9			
EYE	# Ex	10	0	0	10			
HARDERIAN GLAND	# Ex	10	0	0	10			
Infiltrate, cellular		4 (40)	0	0	4 (40)			

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SECTION III
SEVERITY SUMMARY TABLE

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Severity Summary Table

DRAFT

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PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

WEEKS: 3-14

SEX: MALE

GROUP:

NUMBER OF ANIMALS:

Veh Con
10

0.5mbkd
10

1.5mbkd
10

4.5mbkd
10

		#	SEV	#	SEV	#	SEV	#	SEV
BRAIN	# Ex	10		0		1		10	
Choroid plexus, hemorrhage		1	0.20	0		0		0	
Lateral ventricle, hemorrhage		1	0.10	0		0		0	
PITUITARY GLAND	# Ex	10		0		1		8	
SPINAL CORD, THORACIC	# Ex	10		0		1		10	
PANCREAS	# Ex	10		0		1		10	
SALIVARY GLAND	# Ex	10		0		1		10	
THYMUS	# Ex	10		10		10		7	
Depletion, lymphocyte		0		0		1	0.40	4	1.57
Hemorrhage		0		2	0.20	0		1	0.43
ADRENAL GLAND	# Ex	10		0		1		10	
Cortex, congestion		0		0		0		1	0.10
Cortex, vacuolation, cytoplasm		6	0.60	0		0		4	0.40
ESOPHAGUS	# Ex	10		0		1		10	
Inflammation, chronic		1	0.10	0		0		0	
Inflammation, chronic-active		0		0		1	4.00	0	
Inflammation, subacute		0		0		0		1	0.10
PARATHYROID GLAND	# Ex	10		0		1		8	
THYROID GLAND	# Ex	10		0		1		10	

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PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Severity Summary Table

DRAFT

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PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

WEEKS: 3-14

SEX: MALE

GROUP:

NUMBER OF ANIMALS:

Veh Con

10

0.5mbkd

10

1.5mbkd

10

4.5mbkd

10

	#	SEV	#	SEV	#	SEV	#	SEV
TRACHEA	# Ex	10	0		1		10	
AORTA	# Ex	10	0		1		10	
COLON	# Ex	10	0		1		10	
DUODENUM	# Ex	10	0		0		8	
HEART	# Ex	10	0		1		10	
Cardiomyopathy		9 1.20	0		0		3 0.30	
Inflammation, subacute		0	0		0		1 0.20	
Myocard, inflam, chr-act		0	0		1 2.00		0	
Pericard, inflam, chr-act		0	0		1 4.00		0	
STOMACH	# Ex	10	0		1		10	
Forestomach, inflam, acute		0	0		0		1 0.10	
JEJUNUM	# Ex	10	0		0		8	
LIVER	# Ex	10	10		10		10	
Bile duct, hyperplasia		0	0		0		1 0.20	
Hepatocyte, degeneration		0	0		4 0.40		10 2.70	
Hepatocyte, necrosis		0	0		1 0.10		10 1.70	
Infiltrate, cellular		1 0.10	2 0.20		0		0	
Necrosis, focal		1 0.10	0		0		0	
SPLEEN	# Ex	10	0		1		10	
Depletion, lymphocyte		0	0		0		1 0.30	
Pigment, hemosiderin		0	0		1 2.00		0	

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Severity Summary Table

D R A F T

PAGE 27

PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

WEEKS: 3-14

SEX: MALE

GROUP:

Veh Con

0.5mbkd

1.5mbkd

4.5mbkd

NUMBER OF ANIMALS:

10

10

10

10

	#	SEV	#	SEV	#	SEV	#	SEV
LUNG	# Ex	10	10	10	10	10	10	10
Alveolar histiocytosis		1 0.10	4 0.40	8 1.40	10 1.50			
Congestion		0	0	1 0.30	1 0.20			
Hemorrhage		1 0.10	4 0.70	3 0.30	0			
Inflammation, subacute		7 0.70	3 0.30	2 0.20	0			
Pleura, inflam, chr-act		0	0	1 0.40	0			
Pleura, inflam, chronic, fr bd		0	1 0.30	0	0			
KIDNEY	# Ex	10	0	1	10			
Nephropathy		0	0	0	3 0.50			
Renal tubule, casts, proteinic		1 0.10	0	0	0			
Renal tubule, dilatation		2 0.20	0	0	0			
Renal tubule, epith, basophil		1 0.10	0	0	0			
Renal tubule, epith, regenerat		1 0.10	0	0	0			
LYMPH NODE, MESENTERIC	# Ex	10	0	1	10			
URINARY BLADDER	# Ex	10	0	1	10			
Mucosa, inflammation, acute		0	0	0	2 0.20			
Mucosa, ulcer		0	0	0	1 0.10			
PROSTATE	# Ex	10	0	1	10			
Infiltrate, cellular		1 0.10	0	0	1 0.10			
SKIN	# Ex	10	0	1	10			
MAMMARY GLAND	# Ex	10	0	0	10			
Atrophy		0	0	0	2 0.50			
CECUM	# Ex	10	0	0	9			

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PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Severity Summary Table

DRAFT

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PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

WEEKS: 3-14

SEX: MALE

GROUP:

NUMBER OF ANIMALS:

Veh Con
10

0.5mbkd
10

1.5mbkd
10

4.5mbkd
10

	#	SEV	#	SEV	#	SEV	#	SEV
ILEUM	# Ex	10	0	0	0	9		
RECTUM	# Ex	10	0	0	10			
SCIATIC NERVE	# Ex	10	0	0	7			
SKELETAL MUSCLE	# Ex	10	0	1	10			
EPIDIDYMIS	# Ex	10	0	1	10			
Granuloma, sperm		0	0	0	1 0.30			
Hypospermia		0	0	0	1 0.20			
SEMINAL VESICLE	# Ex	10	0	1	10			
TESTIS	# Ex	10	0	1	10			
Atrophy		0	0	0	1 0.10			
DIAPHRAGM	# Ex	10	0	1	9			
Inflammation, chronic-active		0	0	1 4.00	0			
TONGUE	# Ex	10	0	1	10			
FEMUR	# Ex	10	0	1	10			
BONE MARROW	# Ex	10	0	1	10			
Hyperplasia, myeloid		0	0	1 2.00	0			

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PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Severity Summary Table

DRAFT

PAGE 29

PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

WEEKS: 3-14

SEX: MALE

GROUP:

Veh Con

0.5mbkd

1.5mbkd

4.5mbkd

NUMBER OF ANIMALS:

10

10

10

10

	#	SEV	#	SEV	#	SEV	#	SEV
EYE	# Ex	10	0		0		9	
HARDERIAN GLAND	# Ex	10	0		1		10	
Infiltrate, cellular		5 0.70	0		0		1 0.10	
Inflammation, chronic		1 0.10	0		0		0	

* Severity calculated by the number of tissues examined.

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PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Severity Summary Table

DRAFT

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PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

WEEKS: 3-14

SEX: FEMALE

GROUP:

Veh Con

0.5mbkd

1.5mbkd

4.5mbkd

NUMBER OF ANIMALS:

10

10

10

10

		#	SEV	#	SEV	#	SEV	#	SEV
BRAIN	# Ex	10		0		0		10	
Lateral ventricle, hemorrhage		1	0.10	0		0		0	
PITUITARY GLAND	# Ex	10		0		0		10	
SPINAL CORD, THORACIC	# Ex	10		0		0		10	
PANCREAS	# Ex	10		0		0		10	
SALIVARY GLAND	# Ex	10		0		0		10	
THYMUS	# Ex	10		0		0		10	
ADRENAL GLAND	# Ex	10		0		0		10	
Cortex, vacuolation, cytoplasm		0		0		0		1	0.10
ESOPHAGUS	# Ex	10		0		0		10	
PARATHYROID GLAND	# Ex	10		0		0		8	
THYROID GLAND	# Ex	10		0		0		10	
TRACHEA	# Ex	10		0		0		10	
Infiltrate, cellular		0		0		0		1	0.10
AORTA	# Ex	10		0		0		10	

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Severity Summary Table

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PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

WEEKS: 3-14

SEX: FEMALE

GROUP:

NUMBER OF ANIMALS:

Veh Con
10

0.5mbkd
10

1.5mbkd
10

4.5mbkd
10

	#	SEV	#	SEV	#	SEV	#	SEV
COLON	# Ex	10	0		0		10	
DUODENUM	# Ex	10	0		0		10	
HEART	# Ex	10	0		0		10	
Cardiomyopathy		3 0.30	0		0		3 0.30	
STOMACH	# Ex	10	0		0		10	
JEJUNUM	# Ex	10	0		0		10	
LIVER	# Ex	10	0		0		10	
Necrosis, focal		2 0.20	0		0		0	
SPLEEN	# Ex	10	10		10		10	
Extramedullary hematopoiesis		0	0		0		1 0.10	
Pigment, hemosiderin		0	0		0		9 1.20	
LUNG	# Ex	10	10		10		10	
Alveolar histiocytosis		0	1 0.10		9 1.40		10 2.00	
Hemorrhage		2 0.20	2 0.20		1 0.10		0	
Inflammation, subacute		2 0.20	0		1 0.10		0	
KIDNEY	# Ex	10	0		0		10	
Cortex, fibrosis		1 0.10	0		0		0	
Nephrocalcinosis		9 0.90	0		0		6 0.60	
Renal tubule, casts, proteinic		0	0		0		1 0.10	
Renal tubule, dilatation		1 0.10	0		0		0	

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Severity Summary Table

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PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

WEEKS: 3-14

SEX: FEMALE

GROUP:

NUMBER OF ANIMALS:

Veh Con
10

0.5mbkd
10

1.5mbkd
10

4.5mbkd
10

	#	SEV	#	SEV	#	SEV	#	SEV
LYMPH NODE, MESENTERIC	# Ex	10	0	0	0	10		
URINARY BLADDER	# Ex	10	0	0	0	10		
SKIN	# Ex	10	0	0	0	10		
MAMMARY GLAND	# Ex	10	0	0	0	10		
CECUM	# Ex	10	0	0	0	10		
ILEUM	# Ex	10	0	0	0	10		
RECTUM	# Ex	10	0	0	0	10		
SCIATIC NERVE	# Ex	10	0	0	0	10		
SKELETAL MUSCLE	# Ex	10	0	0	0	10		
OVARY	# Ex	10	0	0	0	10		
UTERUS	# Ex	10	0	0	0	10		
Dilatation		1 0.10	0	0	0	3 0.60		
VAGINA	# Ex	9	0	0	0	10		
DIAPHRAGM	# Ex	10	0	0	0	10		

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Severity Summary Table

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PROJECT ID. NO: TRL107

FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead,
Accidental Death

WEEKS: 3-14

SEX: FEMALE

GROUP:

Veh Con

0.5mbkd

1.5mbkd

4.5mbkd

NUMBER OF ANIMALS:

10

10

10

10

	#	SEV	#	SEV	#	SEV	#	SEV
TONGUE	# Ex	10	0		0		10	
FEMUR	# Ex	10	0		0		9	
BONE MARROW	# Ex	10	0		0		9	
EYE	# Ex	10	0		0		10	
HARDERIAN GLAND	# Ex	10	0		0		10	
Infiltrate, cellular		4	0.40		0		4	0.40

* Severity calculated by the number of tissues examined.

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SECTION IV
TABULATED ANIMAL DATA

PATHOLOGY ASSOCIATES, INC.
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Tabulated Animal Data

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: Veh Con SEX: MALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	301	302	303	304	305	306	307	308	309	310
BRAIN	N	N	N		N	N	N		N	N
Choroid plexus, hemorrhage	-	-	-	2	-	-	-	-	-	-
Lateral ventricle, hemorrhage	-	-	-	-	-	-	-	1	-	-
PITUITARY GLAND		N			N	N	N		N	N
Pars distalis, cyst	P	-	P	P	-	-	-	P	-	-
SPINAL CORD, THORACIC	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N	N	N	N	N	N	N	N	N
ADRENAL GLAND	N			N					N	N
Cortex, vacuolation, cytoplasm	-	1	1	-	1	1	1	1	-	-
ESOPHAGUS	N	N	N		N	N	N	N	N	N
Inflammation, chronic	-	-	-	1	-	-	-	-	-	-
PARATHYROID GLAND	N	N	N	N	N	N	N	N	N	N
THYROID GLAND	N	N	N	N	N	N	N	N	N	N

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Tabulated Animal Data

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PAGE 36

PROJECT ID: TRL107
WEEKS: 3-14

GROUP: Veh Con SEX: MALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	301	302	303	304	305	306	307	308	309	310
TRACHEA	N	N	N	N	N	N	N	N	N	N
AORTA	N	N	N	N	N	N	N	N	N	N
COLON	N	N	N	N	N	N	N	N	N	N
DUODENUM	N	N	N	N	N	N	N	N	N	N
HEART					N					
Cardiomyopathy	1	2	1	1	-	2	1	1	2	1
STOMACH	N	N	N	N	N	N	N	N	N	N
JEJUNUM	N	N	N	N	N	N	N	N	N	N
LIVER	N	N	N	N		N	N	N	N	N
Infiltrate, cellular	-	-	-	-	1	-	-	-	-	-
Necrosis, focal	-	-	-	-	1	-	-	-	-	-
SPLEEN	N	N	N	N	N	N	N	N	N	N
LUNG						N				
Alveolar histiocytosis	-	-	1	-	-	-	-	-	-	-
Hemorrhage	-	1	-	-	-	-	-	-	-	-
Inflammation, subacute	1	-	-	1	1	-	1	1	1	1

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Tabulated Animal Data

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PAGE 37

PROJECT ID: TRL107
WEEKS: 3-14

GROUP: Veh Con SEX: MALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	301	302	303	304	305	306	307	308	309	310
KIDNEY		N	N		N	N	N			N
Renal tubule, casts, proteinic	-	-	-	1	-	-	-	-	-	-
Renal tubule, dilatation	-	-	-	-	-	-	-	1	1	-
Renal tubule, epith, basophil	1	-	-	-	-	-	-	-	-	-
Renal tubule, epith, regenerat	-	-	-	1	-	-	-	-	-	-
LYMPH NODE, MESENTERIC	N	N	N	N	N	N	N	N	N	N
URINARY BLADDER	N		N	N	N	N	N	N	N	N
Calculus	-	P	-	-	-	-	-	-	-	-
PROSTATE	N		N	N	N	N	N	N	N	N
Infiltrate, cellular	-	1	-	-	-	-	-	-	-	-
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N
RECTUM	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Tabulated Animal Data

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: Veh Con SEX: MALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	301	302	303	304	305	306	307	308	309	310
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
EPIDIDYMIS	N	N	N	N	N	N	N	N	N	N
SEMINAL VESICLE	N	N	N	N	N	N	N	N	N	N
TESTIS	N	N	N	N	N	N	N	N	N	N
DIAPHRAGM	N	N	N	N	N	N	N	N	N	N
TONGUE	N	N	N	N	N	N	N	N	N	N
FEMUR	N	N	N	N	N	N	N	N	N	N
BONE MARROW	N	N	N	N	N	N	N	N	N	N
EYE	N	N	N	N	N	N	N	N	N	N
HARDERIAN GLAND					N	N		N		N
Infiltrate, cellular	1	1	2	2	-	-	1	-	-	-
Inflammation, chronic	-	-	-	-	-	-	-	-	1	-

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Tabulated Animal Data

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 0.5mbkd SEX: MALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	321	322	323	324	325	326	327	328	329	330
THYMUS	N	N	N	N	N	N	N		N	
Hemorrhage	-	-	-	-	-	-	-	1	-	1
LIVER		N	N	N	N	N		N	N	N
Infiltrate, cellular	1	-	-	-	-	-	1	-	-	-
LUNG						N			N	
Alveolar histiocytosis	1	-	1	1	-	-	-	-	-	1
Hemorrhage	1	1	-	1	-	-	-	4	-	-
Inflammation, subacute	1	-	-	-	1	-	-	-	-	1
Pleura, inflam, chronic, fr bd	-	-	-	-	-	-	3	-	-	-

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Tabulated Animal Data

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 1.5mbkd SEX: MALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	341	342	343	344	345	346	347	348	349	350
BRAIN	*	N	*	*	*	*	*	*	*	*
PITUITARY GLAND	*	N	*	*	*	*	*	*	*	*
SPINAL CORD, THORACIC	*	N	*	*	*	*	*	*	*	*
PANCREAS	*	N	*	*	*	*	*	*	*	*
SALIVARY GLAND	*	N	*	*	*	*	*	*	*	*
THYMUS	N		N	N	N	N	N	N	N	N
Depletion, lymphocyte	-	4	-	-	-	-	-	-	-	-
ADRENAL GLAND	*	N	*	*	*	*	*	*	*	*
ESOPHAGUS	*		*	*	*	*	*	*	*	*
Inflammation, chronic-active	-	4	-	-	-	-	-	-	-	-
PARATHYROID GLAND	*	N	*	*	*	*	*	*	*	*
THYROID GLAND	*	N	*	*	*	*	*	*	*	*
TRACHEA	*	N	*	*	*	*	*	*	*	*

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Tabulated Animal Data

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 1.5mbkd SEX: MALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	341	342	343	344	345	346	347	348	349	350
AORTA	*	N	*	*	*	*	*	*	*	*
COLON	*	N	*	*	*	*	*	*	*	*
DUODENUM	*	A	*	*	*	*	*	*	*	*
HEART	*		*	*	*	*	*	*	*	*
Myocard, inflam, chr-act	-	2	-	-	-	-	-	-	-	-
Pericard, inflam, chr-act	-	4	-	-	-	-	-	-	-	-
STOMACH	*	N	*	*	*	*	*	*	*	*
JEJUNUM	*	A	*	*	*	*	*	*	*	*
LIVER		N	N		N	N	N		N	
Hepatocyte, degeneration	1	-	-	1	-	-	-	1	-	1
Hepatocyte, necrosis	1	-	-	-	-	-	-	-	-	-
SPLEEN	*		*	*	*	*	*	*	*	*
Pigment, hemosiderin	-	2	-	-	-	-	-	-	-	-

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Tabulated Animal Data

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 1.5mbkd SEX: MALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	341	342	343	344	345	346	347	348	349	350
LUNG										N
Alveolar histiocytosis	2	2	2	2	1	2	2	-	1	-
Congestion	-	3	-	-	-	-	-	-	-	-
Hemorrhage	-	-	-	-	-	-	1	1	1	-
Inflammation, subacute	-	-	-	-	-	1	-	1	-	-
Pleura, inflam, chr-act	-	4	-	-	-	-	-	-	-	-
KIDNEY	*	N	*	*	*	*	*	*	*	*
LYMPH NODE, MESENTERIC	*	N	*	*	*	*	*	*	*	*
URINARY BLADDER	*	N	*	*	*	*	*	*	*	*
PROSTATE	*	N	*	*	*	*	*	*	*	*
SKIN	*	N	*	*	*	*	*	*	*	*
MAMMARY GLAND	*	U	*	*	*	*	*	*	*	*
CECUM	*	A	*	*	*	*	*	*	*	*
ILEUM	*	A	*	*	*	*	*	*	*	*
RECTUM	*	A	*	*	*	*	*	*	*	*

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Tabulated Animal Data

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 1.5mbkd SEX: MALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	341	342	343	344	345	346	347	348	349	350
SCIATIC NERVE	*	U	*	*	*	*	*	*	*	*
SKELETAL MUSCLE	*	N	*	*	*	*	*	*	*	*
EPIDIDYMIS	*	N	*	*	*	*	*	*	*	*
SEMINAL VESICLE	*	N	*	*	*	*	*	*	*	*
TESTIS	*	N	*	*	*	*	*	*	*	*
DIAPHRAGM	*		*	*	*	*	*	*	*	*
Inflammation, chronic-active	-	4	-	-	-	-	-	-	-	-
TONGUE	*	N	*	*	*	*	*	*	*	*
FEMUR	*	N	*	*	*	*	*	*	*	*
BONE MARROW	*		*	*	*	*	*	*	*	*
Hyperplasia, myeloid	-	2	-	-	-	-	-	-	-	-
EYE	*	A	*	*	*	*	*	*	*	*
HARDERIAN GLAND	*	N	*	*	*	*	*	*	*	*

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

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Tabulated Animal Data

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 1.5mbkd SEX: MALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	341	342	343	344	345	346	347	348	349	350
OTHER TISSUES AND LESIONS:										
SKL MUS, VNT - Inflamm, chr-act	-	3	-	-	-	-	-	-	-	-

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Tabulated Animal Data

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 4.5mbkd SEX: MALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	361	362	363	364	365	366	367	368	369	370
BRAIN	N	N	N	N	N	N	N	N	N	N
PITUITARY GLAND	N	N	N	N	N	U	U	N	N	N
SPINAL CORD, THORACIC	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
THYMUS				N	N	U	U	U	N	
Depletion, lymphocyte	2	1	4	-	-	-	-	-	-	4
Hemorrhage	-	-	3	-	-	-	-	-	-	-
ADRENAL GLAND	N		N				N	N	N	
Cortex, congestion	-	-	-	-	-	1	-	-	-	-
Cortex, vacuolation, cytoplasm	-	1	-	1	1	-	-	-	-	1
ESOPHAGUS	N	N	N	N	N	N	N		N	N
Inflammation, subacute	-	-	-	-	-	-	-	1	-	-
PARATHYROID GLAND	N	N	N	N	N	U	N	N	N	U
THYROID GLAND	N	N	N	N	N	N	N	N	N	N

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Tabulated Animal Data

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 4.5mbkd SEX: MALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	361	362	363	364	365	366	367	368	369	370
TRACHEA	N	N	N	N	N	N	N	N	N	N
AORTA	N	N	N	N	N	N	N	N	N	N
COLON	N	N	N	N	N	N	N	N	N	N
DUODENUM	N	N	A	N	N	A	N	N	N	N
HEART	N	N	N		N				N	N
Cardiomyopathy	-	-	-	1	-	1	-	1	-	-
Inflammation, subacute	-	-	-	-	-	-	2	-	-	-
STOMACH	N	N	N	N	N	N		N	N	N
Forestomach, inflam, acute	-	-	-	-	-	-	1	-	-	-
JEJUNUM	N	N	A	N	N	A	N	N	N	N
LIVER										
Bile duct, hyperplasia	-	-	-	-	-	-	-	2	-	-
Hepatocyte, degeneration	3	3	3	3	1	2	3	3	3	3
Hepatocyte, necrosis	2	2	2	2	1	2	2	2	1	1
SPLEEN	N	N		N	N	N	N	N	N	N
Depletion, lymphocyte	-	-	3	-	-	-	-	-	-	-

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Tabulated Animal Data

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PAGE 47

PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 4.5mbkd SEX: MALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	361	362	363	364	365	366	367	368	369	370
LUNG										
Alveolar histiocytosis	1	2	1	2	2	1	1	1	2	2
Congestion	-	-	-	-	-	2	-	-	-	-
KIDNEY	N			N	N	N		N	N	N
Nephropathy	-	2	2	-	-	-	1	-	-	-
LYMPH NODE, MESENTERIC	N	N	N	N	N	N	N	N	N	N
URINARY BLADDER	N	N			N	N	N	N		
Calculus	-	-	-	P	-	-	-	-	-	P
Mucosa, inflammation, acute	-	-	1	-	-	-	-	-	1	-
Mucosa, ulcer	-	-	1	-	-	-	-	-	-	-
PROSTATE	N	N	N	N		N	N	N	N	N
Infiltrate, cellular	-	-	-	-	1	-	-	-	-	-
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N		N	N	N	N	N	N	N	
Atrophy	-	2	-	-	-	-	-	-	-	3
CECUM	N	N	A	N	N	N	N	N	N	N
ILEUM	N	N	A	N	N	N	N	N	N	N

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TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Tabulated Animal Data

DRAFT

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 4.5mbkd SEX: MALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	361	362	363	364	365	366	367	368	369	370
RECTUM	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	U	N	N	N	N	U	U	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
EPIDIDYMIS	N	N	N	N	N	N	N		N	N
Granuloma, sperm	-	-	-	-	-	-	-	3	-	-
Hypospermia	-	-	-	-	-	-	-	2	-	-
SEMINAL VESICLE	N	N	N	N	N	N	N	N	N	N
TESTIS	N		N	N	N	N	N	N	N	N
Atrophy	-	1	-	-	-	-	-	-	-	-
DIAPHRAGM	N	N	N	N	N	N	N	N	U	N
TONGUE	N	N	N	N	N	N	N	N	N	N
FEMUR	N	N	N	N	N	N	N	N	N	N
BONE MARROW	N	N	N	N	N	N	N	N	N	N
EYE	N	N	A	N	N	N	N	N	N	N

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Tabulated Animal Data

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 4.5mbkd SEX: MALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	361	362	363	364	365	366	367	368	369	370
HARDERIAN GLAND	N		N	N	N	N	N	N	N	N
Infiltrate, cellular	-	1	-	-	-	-	-	-	-	-

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: Veh Con SEX: FEMALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	311	312	313	314	315	316	317	318	319	320
BRAIN	N	N	N		N	N	N	N	N	N
Lateral ventricle, hemorrhage	-	-	-	1	-	-	-	-	-	-
PITUITARY GLAND	N	N	N	N	N	N	N		N	N
Pars distalis, cyst	-	-	-	-	-	-	-	P	-	-
SPINAL CORD, THORACIC	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N	N	N	N	N	N	N	N	N
ADRENAL GLAND	N	N	N	N	N	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	N	N	N	N	N	N	N	N	N	N
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
TRACHEA	N	N	N	N	N	N	N	N	N	N

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: Veh Con SEX: FEMALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	311	312	313	314	315	316	317	318	319	320
AORTA	N	N	N	N	N	N	N	N	N	N
COLON	N	N	N	N	N	N	N	N	N	N
DUODENUM	N	N	N	N	N	N	N	N	N	N
HEART	N	N		N	N	N		N	N	
Cardiomyopathy	-	-	1	-	-	-	1	-	-	1
STOMACH	N	N	N	N	N	N	N	N	N	N
JEJUNUM	N	N	N	N	N	N	N	N	N	N
LIVER	N	N	N		N	N	N		N	N
Necrosis, focal	-	-	-	1	-	-	-	1	-	-
SPLEEN	N	N	N	N	N	N	N	N	N	N
LUNG	N	N		N		N	N	N	N	
Hemorrhage	-	-	-	-	1	-	-	-	-	1
Inflammation, subacute	-	-	1	-	1	-	-	-	-	-

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: Veh Con SEX: FEMALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	311	312	313	314	315	316	317	318	319	320
KIDNEY	N									
Cortex, fibrosis	-	-	-	-	-	-	-	1	-	-
Nephrocalcinosis	-	1	1	1	1	1	1	1	1	1
Renal tubule, dilatation	-	-	-	-	-	-	-	1	-	-
LYMPH NODE, MESENTERIC	N	N	N	N	N	N	N	N	N	N
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N
RECTUM	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
OVARY	N	N	N	N	N	N	N	N	N	N

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Tabulated Animal Data

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: Veh Con SEX: FEMALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	311	312	313	314	315	316	317	318	319	320
UTERUS		N	N	N	N	N	N	N	N	N
Dilatation	1	-	-	-	-	-	-	-	-	-
VAGINA	N	N	N	N	N	N	N	N	N	U
DIAPHRAGM	N	N	N	N	N	N	N	N	N	N
TONGUE	N	N	N	N	N	N	N	N	N	N
FEMUR	N	N	N	N	N	N	N	N	N	N
BONE MARROW	N	N	N	N	N	N	N	N	N	N
EYE	N	N	N	N	N	N	N	N	N	N
HARDERIAN GLAND	N	N	N				N	N		N
Infiltrate, cellular	-	-	-	1	1	1	-	-	1	-

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Tabulated Animal Data

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 0.5mbkd SEX: FEMALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	331	332	333	334	335	336	337	338	339	340
SPLEEN	N	N	N	N	N	N	N	N	N	N
LUNG		N		N	N	N	N	N	N	N
Alveolar histiocytosis	1	-	-	-	-	-	-	-	-	-
Hemorrhage	1	-	1	-	-	-	-	-	-	-

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Tabulated Animal Data

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 1.5mbkd SEX: FEMALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	351	352	353	354	355	356	357	358	359	360
SPLEEN	N	N	N	N	N	N	N	N	N	N
LUNG										
Alveolar histiocytosis	2	2	1	-	1	2	1	1	2	2
Hemorrhage	-	-	-	1	-	-	-	-	-	-
Inflammation, subacute	1	-	-	-	-	-	-	-	-	-

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Tabulated Animal Data

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 4.5mbkd SEX: FEMALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	371	372	373	374	375	376	377	378	379	380
BRAIN	N	N	N	N	N	N	N	N	N	N
PITUITARY GLAND	N		N			N	N	N	N	N
Pars distalis, cyst	-	P	-	P	P	-	-	-	-	-
SPINAL CORD, THORACIC	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N	N	N	N	N	N	N	N	N
ADRENAL GLAND	N	N	N	N	N	N	N	N		N
Cortex, vacuolation, cytoplasm	-	-	-	-	-	-	-	-	1	-
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	N	N	U	N	N	N	N	N	N	U
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
TRACHEA	N	N		N	N	N	N	N	N	N
Infiltrate, cellular	-	-	1	-	-	-	-	-	-	-

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 4.5mbkd SEX: FEMALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	371	372	373	374	375	376	377	378	379	380
AORTA	N	N	N	N	N	N	N	N	N	N
COLON	N	N	N	N	N	N	N	N	N	N
DUODENUM	N	N	N	N	N	N	N	N	N	N
HEART	N	N		N	N		N	N	N	
Cardiomyopathy	-	-	1	-	-	1	-	-	-	1
STOMACH	N	N	N	N	N	N	N	N	N	N
JEJUNUM	N	N	N	N	N	N	N	N	N	N
LIVER	N	N	N	N	N	N	N	N	N	N
SPLEEN				N						
Extramedullary hematopoiesis	-	1	-	-	-	-	-	-	-	-
Pigment, hemosiderin	2	2	1	-	1	1	1	1	2	1
LUNG										
Alveolar histiocytosis	2	2	2	2	2	2	2	2	2	2
KIDNEY	N	N	N					N		
Nephrocalcinosis	-	-	-	1	1	1	1	-	1	1
Renal tubule, casts, proteinic	-	-	-	-	-	-	1	-	-	-

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Tabulated Animal Data

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PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 4.5mbkd SEX: FEMALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	371	372	373	374	375	376	377	378	379	380
LYMPH NODE, MESENTERIC	N	N	N	N	N	N	N	N	N	N
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N
RECTUM	N	N	N	N	N	N	N	N	N	N
SCIATIC NERVE	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
OVARY	N	N	N	N	N	N	N	N	N	N
UTERUS		N		N	N	N	N		N	N
Dilatation	2	-	1	-	-	-	-	3	-	-

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Tabulated Animal Data

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PAGE 59

PROJECT ID: TRL107
WEEKS: 3-14

GROUP: 4.5mbkd SEX: FEMALE
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID:	371	372	373	374	375	376	377	378	379	380
VAGINA	N	N	N	N	N	N	N	N	N	N
DIAPHRAGM	N	N	N	N	N	N	N	N	N	N
TONGUE	N	N	N	N	N	N	N	N	N	N
FEMUR	N	N	N	N	N	N	N	U	N	N
BONE MARROW	N	N	N	N	N	N	N	U	N	N
EYE	N	N	N	N	N	N	N	N	N	N
HARDERIAN GLAND	N	N	N	N				N	N	
Infiltrate, cellular	-	-	-	-	1	1	1	-	-	1

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SECTION V

CORRELATION OF GROSS AND MICROSCOPIC (MICRO) FINDINGS

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: Veh Con SEX: MALE PAGE 61
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 301 PATHOLOGY ID. NO: TI107-301 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 302 PATHOLOGY ID. NO: TI107-302 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>URINARY BLADDER - CALCULUS URINARY BLADDER - Calculus

ANIMAL ID: 303 PATHOLOGY ID. NO: TI107-303 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 304 PATHOLOGY ID. NO: TI107-304 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: Veh Con SEX: MALE PAGE 62
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 305 PATHOLOGY ID. NO: TI107-305 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 306 PATHOLOGY ID. NO: TI107-306 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 307 PATHOLOGY ID. NO: TI107-307 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 308 PATHOLOGY ID. NO: TI107-308 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: Veh Con SEX: MALE PAGE 63
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 309 PATHOLOGY ID. NO: TI107-309 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 310 PATHOLOGY ID. NO: TI107-310 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

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THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 0.5mbkd SEX: MALE PAGE 64
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 321 PATHOLOGY ID. NO: TI107-321 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 322 PATHOLOGY ID. NO: TI107-322 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 323 PATHOLOGY ID. NO: TI107-323 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 324 PATHOLOGY ID. NO: TI107-324 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 0.5mbkd SEX: MALE PAGE 65
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 325 PATHOLOGY ID. NO: TI107-325 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 326 PATHOLOGY ID. NO: TI107-326 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 327 PATHOLOGY ID. NO: TI107-327 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

>LUNG, APICAL LOBE - LESION, DIFFUSE, PALE, FIRM	LUNG - Pleura, inflam, chronic, fr bd
>LYMPH NODE, MEDIASTINAL - ENLARGED, MULTIPLE, DARK	Not required by protocol

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 0.5mbkd SEX: MALE PAGE 66
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 328 PATHOLOGY ID. NO: TI107-328 PATHOLOGIST: MJT
ANIMAL FATE: Accidental Death
WEEKS ON TEST: 13

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 329 PATHOLOGY ID. NO: TI107-329 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 330 PATHOLOGY ID. NO: TI107-330 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 1.5mbkd SEX: MALE PAGE 67
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 341 PATHOLOGY ID. NO: TI107-341 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

ANIMAL ID: 342 PATHOLOGY ID. NO: TI107-342 PATHOLOGIST: MJT
ANIMAL FATE: Found Dead
WEEKS ON TEST: 13

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, DIFFUSE, LUNG - Congestion, LUNG - Pleura,
DARK, RED inflam, chr-act
>HEART, PERICARDIUM - ADHESION, HEART - Pericard, inflam, chr-act
DIFFUSE, FLAT, WHITE, FIBRINOUS
>CAVITIES, PERICARDIAL - FLUID, 1 No section taken
ML, RED, WATERY
>CAVITIES, THORACIC - FLUID, 8 ML, No section taken
DARK RED
>ESOPHAGUS - DILATATION, DIFFUSE No corresponding lesion
>SKIN, INGUINAL - PIGMENTATION, No corresponding lesion
MASS, 1, RED, BLACK, RUBBERY, 40X10
MM
>TISSUE NOS, VENTRAL - LESION, 1 SKL MUS, VNT - Inflam, chr-act
LINEAR, BROWN, TAN, VISCOUS, 120 MM

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 1.5mbkd SEX: MALE PAGE 68
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 342 PATHOLOGY ID. NO: TI107-342 PATHOLOGIST: MJT
ANIMAL FATE: Found Dead WEEKS ON TEST: 13

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LIVER - FOCUS, MULTIPLE, IRREGULAR, PALE No corresponding lesion
>DIAPHRAGM - ACCUMULATION, DIFFUSE, WHITE, FIBRINOUS DIAPHRAGM - Inflammation, chronic-active

ANIMAL ID: 343 PATHOLOGY ID. NO: TI107-343 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, IRREGULAR, LINEAR, WHITE LUNG - Alveolar histiocytosis

ANIMAL ID: 344 PATHOLOGY ID. NO: TI107-344 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, IRREGULAR, LINEAR, WHITE LUNG - Alveolar histiocytosis

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 1.5mbkd SEX: MALE PAGE 69
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 345 PATHOLOGY ID. NO: TI107-345 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 346 PATHOLOGY ID. NO: TI107-346 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

ANIMAL ID: 347 PATHOLOGY ID. NO: TI107-347 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

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D R A

Correlation of Gross & Micro Findings

PROJECT ID: TRL107 GROUP: 1.5mbkd SEX: MALE PAGE 70
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 348 PATHOLOGY ID. NO: TI107-348 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>KIDNEY, BILATERAL - CYST, MULTIPLE, Not required by protocol
ROUND, CLEAR, 1 MM

ANIMAL ID: 349 PATHOLOGY ID. NO: TI107-349 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

ANIMAL ID: 350 PATHOLOGY ID. NO: TI107-350 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 4.5mbkd SEX: MALE PAGE 71
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 361 PATHOLOGY ID. NO: TI107-361 PATHOLOGIST: MJT
ANIMAL FATE: Moribund Sacrifice
WEEKS ON TEST: 5

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LIVER - LESION, MOTTLED LIVER - Hepatocyte, degeneration

ANIMAL ID: 362 PATHOLOGY ID. NO: TI107-362 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

ANIMAL ID: 363 PATHOLOGY ID. NO: TI107-363 PATHOLOGIST: MJT
ANIMAL FATE: Found Dead
WEEKS ON TEST: 4

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LIVER, PARENCHYMA - LESION, LIVER - Hepatocyte, degeneration,
DIFFUSE, PALE LIVER - Hepatocyte, necrosis

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 4.5mbkd SEX: MALE PAGE 72
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 364 PATHOLOGY ID. NO: TI107-364 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

ANIMAL ID: 365 PATHOLOGY ID. NO: TI107-365 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

ANIMAL ID: 366 PATHOLOGY ID. NO: TI107-366 PATHOLOGIST: MJT
ANIMAL FATE: Found Dead
WEEKS ON TEST: 4

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 4.5mbkd SEX: MALE PAGE 73
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 367 PATHOLOGY ID. NO: TI107-367 PATHOLOGIST: MJT
ANIMAL FATE: Moribund Sacrifice
WEEKS ON TEST: 10

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LIVER, MEDIAN LOBE - PIGMENTATION, LIVER - Hepatocyte, degeneration
1, IRREGULAR, LINEAR, 11 MM

ANIMAL ID: 368 PATHOLOGY ID. NO: TI107-368 PATHOLOGIST: MJT
ANIMAL FATE: Moribund Sacrifice
WEEKS ON TEST: 4

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>INTESTINE, SMALL - ACCUMULATION, No corresponding lesion
FLUID, CLEAR, WATERY
>LIVER, PARENCHYMA - LESION, LIVER - Bile duct, hyperplasia,
DIFFUSE, PALE LIVER - Hepatocyte, degeneration,
LIVER - Hepatocyte, necrosis
>INTESTINE, LARGE - ACCUMULATION, No corresponding lesion
FLUID, CLEAR, WATERY
>STOMACH - ACCUMULATION, FLUID, No corresponding lesion
CLEAR, WATERY

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 4.5mbkd SEX: MALE PAGE 74
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 369 PATHOLOGY ID. NO: TI107-369 PATHOLOGIST: MJT
ANIMAL FATE: Moribund Sacrifice
WEEKS ON TEST: 3

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>LIVER, PARENCHYMA - LESION, DIFFUSE, PALE	LIVER - Hepatocyte, degeneration, LIVER - Hepatocyte, necrosis
>LIVER, PARENCHYMA - LESION, DIFFUSE, IRREGULAR, DARK, 0.5 MM	LIVER - Hepatocyte, degeneration, LIVER - Hepatocyte, necrosis

ANIMAL ID: 370 PATHOLOGY ID. NO: TI107-370 PATHOLOGIST: MJT
ANIMAL FATE: Moribund Sacrifice
WEEKS ON TEST: 5

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>LIVER, PARENCHYMA - LESION, DIFFUSE, PALE	LIVER - Hepatocyte, degeneration, LIVER - Hepatocyte, necrosis

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: Veh Con SEX: FEMALE PAGE 75
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 311 PATHOLOGY ID. NO: TI107-311 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 312 PATHOLOGY ID. NO: TI107-312 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 313 PATHOLOGY ID. NO: TI107-313 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 314 PATHOLOGY ID. NO: TI107-314 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

>LUNG - FOCUS, MULTIPLE, ROUND, WHITE No corresponding lesion

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: Veh Con SEX: FEMALE PAGE 76
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 315 PATHOLOGY ID. NO: TI107-315 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 316 PATHOLOGY ID. NO: TI107-316 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 317 PATHOLOGY ID. NO: TI107-317 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 318 PATHOLOGY ID. NO: TI107-318 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: Veh Con SEX: FEMALE PAGE 77
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 319 PATHOLOGY ID. NO: TI107-319 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 320 PATHOLOGY ID. NO: TI107-320 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 0.5mbkd SEX: FEMALE PAGE 78
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 331 PATHOLOGY ID. NO: TI107-331 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 332 PATHOLOGY ID. NO: TI107-332 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 333 PATHOLOGY ID. NO: TI107-333 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 334 PATHOLOGY ID. NO: TI107-334 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 0.5mbkd SEX: FEMALE PAGE 79
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 335 PATHOLOGY ID. NO: TI107-335 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 336 PATHOLOGY ID. NO: TI107-336 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 337 PATHOLOGY ID. NO: TI107-337 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 338 PATHOLOGY ID. NO: TI107-338 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 0.5mbkd SEX: FEMALE PAGE 80
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 339 PATHOLOGY ID. NO: TI107-339 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 340 PATHOLOGY ID. NO: TI107-340 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>UTERUS, BILATERAL - ENLARGED, Not required by protocol
DIFFUSE

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 1.5mbkd SEX: FEMALE PAGE 81
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 351 PATHOLOGY ID. NO: TI107-351 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

ANIMAL ID: 352 PATHOLOGY ID. NO: TI107-352 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

ANIMAL ID: 353 PATHOLOGY ID. NO: TI107-353 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 1.5mbkd SEX: FEMALE PAGE 82
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 354 PATHOLOGY ID. NO: TI107-354 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 355 PATHOLOGY ID. NO: TI107-355 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

ANIMAL ID: 356 PATHOLOGY ID. NO: TI107-356 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:

>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE
>KIDNEY, BILATERAL - CYST, MULTIPLE, Not required by protocol
ROUND, CLEAR, 1 MM

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 1.5mbkd SEX: FEMALE PAGE 83
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 357 PATHOLOGY ID. NO: TI107-357 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

ANIMAL ID: 358 PATHOLOGY ID. NO: TI107-358 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

ANIMAL ID: 359 PATHOLOGY ID. NO: TI107-359 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE
>UTERUS, BILATERAL - ENLARGED, Not required by protocol
DIFFUSE

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 1.5mbkd SEX: FEMALE PAGE 84
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 360 PATHOLOGY ID. NO: TI107-360 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 4.5mbkd SEX: FEMALE PAGE 85
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 371 PATHOLOGY ID. NO: TI107-371 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

ANIMAL ID: 372 PATHOLOGY ID. NO: TI107-372 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

ANIMAL ID: 373 PATHOLOGY ID. NO: TI107-373 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

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Correlation of Gross & Micro Findings

D R A F T

PROJECT ID: TRL107 GROUP: 4.5mbkd SEX: FEMALE PAGE 86
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 374 PATHOLOGY ID. NO: TI107-374 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

ANIMAL ID: 375 PATHOLOGY ID. NO: TI107-375 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

ANIMAL ID: 376 PATHOLOGY ID. NO: TI107-376 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

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Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 4.5mbkd SEX: FEMALE PAGE 87
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 377 PATHOLOGY ID. NO: TI107-377 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

ANIMAL ID: 378 PATHOLOGY ID. NO: TI107-378 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE
>UTERUS, BILATERAL - ENLARGED, UTERUS - Dilatation
DIFFUSE

ANIMAL ID: 379 PATHOLOGY ID. NO: TI107-379 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD: RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, LUNG - Alveolar histiocytosis
IRREGULAR, LINEAR, WHITE

26-Sep-1994

PATHOLOGY ASSOCIATES, INC.
THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS
TOXICOLOGY RESEARCH LABORATORY, STUDY NUMBER 107

Correlation of Gross & Micro Findings

DRAFT

PROJECT ID: TRL107 GROUP: 4.5mbkd SEX: FEMALE PAGE 88
WEEKS: 3-14
FATES: Terminal Sacrifice, Moribund Sacrifice, Found Dead, Accidental Death

ANIMAL ID: 380 PATHOLOGY ID. NO: TI107-380 PATHOLOGIST: MJT
ANIMAL FATE: Terminal Sacrifice
WEEKS ON TEST: 14

REFERENCE TO NECROPSY RECORD:	RELATED HISTOPATHOLOGY:
>LUNG, BILATERAL - LESION, MULTIPLE, IRREGULAR, LINEAR, WHITE	LUNG - Alveolar histiocytosis

26-Sep-1994

SECTION VI
QUALITY ASSURANCE STATEMENT

QUALITY ASSURANCE STATEMENT

This histopathology project was inspected and audited by the PAI Quality Assurance Unit (QAU) as required by the Good Laboratory Practice (GLP) standards promulgated by the U.S. Food and Drug Administration. The pathology narrative report is an accurate reflection of the recorded data. The following table is a record of the inspections/audits performed and reported by the QAU:

Date of Inspection	Phase Inspected	Date Findings Reported to Management and Study Pathologist
* 01/25/94	Tissue Trimming	01/25/94
** 02/11/94	Processing/Embedding	02/11/94
* 03/17/94	Microtomy	03/17/94
* 03/18/94	Staining	03/18/94
* 03/18/94	Coverslipping	03/18/94
* 03/08/94	Labeling	03/08/94
* 02/28/94	Quality Control/Checkout	02/28/94
** 05/02/94	Individual Animal Data	05/02/94
** 05/02/94	Data Entry	05/02/94
** 05/02/94	Computer Generated Tables	05/02/94
** 05/02/94	Draft Pathology Report	05/02/94
** 05/05/94	Revised Draft Pathology Report	05/05/94
** 09/26/94	Third Draft Pathology Report	09/26/94

* General quarterly phase inspection
** Inspection specific for Study Number

In accordance with the PAI Quality Assurance Division's Standard Operating Procedures, all critical phase inspections are conducted on a random basis quarterly or more frequently. Those general phase inspections listed are the most recent conducted during the period each task associated with this project was performed.



Quality Assurance Unit
PAI Illinois Division

09/26/94

Date

Thirteen Week Oral Toxicity Study of WR242511 in Rats
TRL Study Number 107

DRAFT

APPENDIX 11

Protocol and Protocol Amendments

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS

1.0 PURPOSE OF THE STUDY:

The purpose of this study is to determine specific target organ toxicity, dose-response relationships, and a no adverse effect level of WR242511 administered to CD® rats for thirteen weeks by daily gavage administration.

2.0 SPONSOR:

- 2.1 Name: U.S. Army Medical Materiel
Development Activity
- 2.2 Address: Fort Detrick
Frederick, MD 21702-5009
- 2.3 Representative: George Schieferstein, Ph.D.

3.0 TESTING FACILITY:

- 3.1 Name: Toxicology Research Laboratory (TRL)
- 3.2 Address: University of Illinois at Chicago (UIC)
Department of Pharmacology
1940 W. Taylor St.
Chicago, IL 60612-7353
- 3.3 Study Director: Barry S. Levine, D.Sc., D.A.B.T.

4.0 DATES:

- 4.1 Study Initiation Date
(see 11.0; Protocol Approval):
- 4.2 Proposed Initiation of Dosing: 10/14/93
- 4.3 Proposed Necropsy Dates: 01/13-14/94
- 4.4 Proposed Study Completion Date
(Draft Study Report): 4/15/94

5.0 TEST ARTICLE

- 5.1 Name or Code No: WR242511 Tartrate
Bottle number will be identified in the raw data
- 5.2 TRL Chemical No: 1720614
- 5.3 Physical Description: Yellow powder
- 5.4 Stability and Handling of Test Article:
- 5.4.1 Temperature: -15 to -20°C.
- 5.4.2 Humidity: Ambient conditions at -20 to -15°C in a freezer
- 5.4.3 Light: Protect from light.
- 5.4.4 Special Requirements: None.
- 5.5 Special Handling Procedures: Standard safety precautions will be followed including gloves, eye protection, mask, and lab coats.
- 5.6 Log of Test Article: The amount, date, identity of person(s) removing aliquots and the purpose for which each aliquot of the test article was removed from the batch will be documented. At termination of the study, all unused test article will be returned to the Sponsor.

6.0 PERSONNEL:

Study Director	Barry S. Levine, D.Sc., D.A.B.T.
Toxicologist	Clyde W. Wheeler, Ph.D.
Pathologist	Michael J. Tomlinson, D.V.M., Ph.D., D.A.C.V.P.
Pathology Support	Ralph M. Bunte, D.V.M., D.A.C.V.P.
Analytical Chemist	Adam Negruz, Ph.D.
Clinical Veterinarian	James E. Artwohl, D.V.M., M.S., D.A.C.L.A.M.
Veterinarian Support	Documented in raw data
Ophthalmologist	Samuel J. Vainisi, D.V.M., D.A.C.V.O.
Tox. Lab Supervisor	Soudabeh Soura, B.S.
Lead Technician	Nancy Dinger, B.S.
Clinical Pathology	Maria Lang, A.H.T., C.V.T.
Chemistry Specialist	Thomas Tolhurst, B.S.
Quality Assurance	Ronald C. Schoenbeck

7.0 TEST SYSTEM:

- 7.1 Species: Rat
- 7.2 Strain: CD® (Virus Antibody Free)
- 7.3 Number and Sex: 40 Males and 40 Females
- 7.4 Age of Animals: Approximately 7 weeks old at dosing initiation.
- 7.5 Weight of Animals: Approximately 200 - 250 g (males) and approximately 150 - 200 g (females) at dosing initiation.
- 7.6 Source of Animals: Charles River Breeding Laboratories. The specific breeding facility will be documented in the raw data.
- 7.7 Justification for Selection of Test System: The rat is a standard and accepted rodent species for toxicology studies, and is specified by the Sponsor.
- 7.8 Procedure for Unique Identification of Test System: Upon arrival, each animal will be given a study-unique quarantine/pretest number. During the test animal selection process, each test animal will be assigned a test animal number unique to it within the population making up the study. This number will appear as an ear tag and will also appear on a cage card visible on the front of each cage. The cage card will additionally contain the study number, test article identification, treatment group number and dose level. Cage cards will be color-coded as a function of treatment group. Raw data records and specimens will also be identified by the unique test animal number.
- 7.9 Housing: The animals will be housed in an AAALAC-accredited facility. Animals will be singly housed in polycarbonate cages with Anderson-bed-a-cob bedding (Heinold, Kankakee, Illinois) in a temperature (65-78°F) and humidity (30-70%) controlled room with a 14 hour light/10 hour dark cycle. The cage size, 840 cm² area and 20 cm height, is adequate to house rats at the upper weight range as described in the Guide for the Care and Use of Laboratory Animals, DHHS (NIH) No. 86.23. All animals will be routinely transferred to clean cages with fresh bedding once weekly.
- 7.10 Quarantine Procedure: Animals will be quarantined for approximately one week. During that time, the animals will be observed daily for signs of illness, and all unusual observations will be reported to the Study Director, Toxicologist or Clinical Veterinarian. Animals

will be examined during quarantine and approved for use by the Clinical Veterinarian prior to being placed on test. Any sickly animals will be eliminated prior to the test animal selection process. If a selected animal appears sickly prior to initiation of treatment, it will be replaced by a healthy animal prior to initiation of treatment under the direction of the Study Director or Toxicologist. Quarantine release will be documented on the Clinical Veterinarian Log by the veterinarian prior to study initiation.

- 7.11 Food: Purina Certified Rodent Chow No. 5002 (Ralston Purina Company, St. Louis, MO) will be provided *ad libitum* from arrival until termination, except during an approximate 16-20 hour fast prior to blood collection for clinical pathology and/or necropsy.
- 7.12 Water: Tap water from an automatic watering system in which the room distribution lines are flushed daily will be provided *ad libitum* from arrival until termination. The water is untreated with additional chlorine or HCl.
- 7.13 There are no known contaminants in the feed or water which are expected to influence the study. A copy of the feed certification will be kept with the study records. The results of bimonthly comprehensive chemical analyses of Chicago water are documented in files maintained by Quality Assurance.

8.0 EXPERIMENTAL DESIGN:

8.1 Treatment Groups:

<u>Treatment Group</u>	<u>Treatment</u>	<u>Dose Level (mg base/kg/day)</u>	<u>Number of Males</u>	<u>Number of Females</u>
1	Vehicle	0	10	10
2	WR242511	0.5	10	10
3	WR242511	1.5	10	10
4	WR242511	4.5	10	10

Dose levels were selected by Sponsor based upon the results of a two week oral dose range-finding study in rats (UIC/TRL Study No. 106).

The number of animals/sex/group is necessary for statistical analyses.

- 8.2 Frequency and Route of Administration of the Test Article: The test article will be administered by gavage once daily starting with Day 0 for at least thirteen weeks. Control animals will receive the test article vehicle. The animals to be sacrificed after the 13 week treatment period will be dosed up to and including the day prior to their scheduled necropsy on Days 91 and 92. Dosing volume will be 5 ml/kg, adjusted on the basis of each animal's most recent body weight. The actual volume (ml) administered will be documented in the raw data.
- 8.3 Justification of Route(s): Oral treatment is the intended clinical route of administration and is specified by the Sponsor.
- 8.4 Procedure to Control Bias during the Assignment of Animals to Treatment Groups: During the quarantine/pretest period, the animals will be randomized by sex into the groups shown in Section 8.1 using a computer-generated randomization procedure on the basis of body weight.
- 8.5 Test Article Vehicle: 1% Methylcellulose/0.2% Tween 80.
- 8.6 Test Article Dosage Form Preparation and Analyses: The dosage formulations for the test article will be prepared daily by diluting a stock formulation (made weekly) to appropriate concentration. Stability and homogeneity data obtained from a previous study (UIC/TRL Study No. 106) indicated that the dosing suspensions are stable for 48 hours at the dosage formulations being tested, and the stock formulation is stable for two weeks. The test article will be prepared by suspending the appropriate quantity of test article in the vehicle using a mortar and pestle. A sample of dosage formulations (including controls) used at the onset of Week 1, 7 and 13 will be analyzed for test article concentration prior to use. Only samples within 10% of their target concentration will be used.
- 8.7 Type and Frequency of Observations, Tests, Analyses and Measurements:
- 8.7.1 Clinical Signs: All animals will be observed once daily for clinical signs of toxicity approximately 1 - 2 hours after dosing. Additionally, all animals will be observed for moribundity/mortality in the afternoon and immediately prior to dosing in the morning.
- 8.7.2 Clinical Observations: All animals will be subjected to a physical examination including examination of eyes and all orifices in Week -1, on Day 0, and weekly thereafter.
- 8.7.3 Body Weight: Body weights of all animals will be recorded at randomization in Week -1, on Day 0, weekly thereafter, and at scheduled termination.

- 8.7.4 Food Consumption: Food consumption for all animals will be measured weekly commencing in Week -1.
- 8.7.5 Ophthalmologic Examinations: All rats will be examined by indirect ophthalmoscopy prior to study initiation and during Week 13.
- 8.7.6 Clinical Pathology: Hematology and clinical chemistry parameters will be measured for all animals during Weeks 5, 9 and 13. The overnight fasted animals will be anesthetized by inhalation of CO₂/O₂ (≈80:20), and approximately 1.5 - 2.0 ml of blood will be collected from the orbital sinus to measure the following parameters. The samples will be processed in the same random order as collected.

Hematology

Erythrocyte count	Mean corpuscular volume (MCV)
Erythrocyte morphology	Mean corpuscular hemoglobin concentration (MCHC)
Heinz bodies	^a Methemoglobin
Hematocrit	Nucleated RBCs
Hemoglobin	Platelet count
Leukocyte count, total and differential	Reticulocyte count
Mean corpuscular hemoglobin (MCH)	

^aTo be measured with a Co-oximeter (Instrumentation Laboratory Model 282). The assay will be performed within one hour of sample collection. The specimens will be kept on wet ice prior to analysis.

Clinical Chemistry

Alanine aminotransferase (ALT/SGPT)	Globulin (calculated)
Albumin	Glucose
Albumin/Globulin ratio (calculated)	Inorganic phosphorus
Alkaline phosphatase	Potassium
Calcium	Sodium
Chloride	Sorbitol dehydrogenase
Cholesterol	Total bile acids
Creatinine	Total protein
	Triglycerides
	Urea nitrogen (BUN)

- 8.7.7 Pathology: All animals which die on test or are sacrificed if moribund will be necropsied on that day. The surviving animals will be sacrificed and necropsied in random order over two consecutive days (Days 91 and 92).

Euthanasia will be accomplished by carbon dioxide asphyxiation, and an extensive necropsy will be performed under the direction and supervision of the pathologist. Terminal body weights will be collected prior to routine sacrifice.

The necropsy procedure will be a thorough and systematic examination and dissection of the animal viscera and carcass, and collection and fixation of the following tissues/organs in 10% neutral buffered formalin.

*Adrenal glands	Pancreas
Animal identification	Pituitary
Aorta	Prostate
*Brain (fore-, mid-, hind-)	Rectum
Cecum	Salivary gland (submaxillary)
Colon	Sciatic nerve
Diaphragm	Seminal vesicles
Duodenum	Skeletal muscle
Esophagus	Skin/Mammary gland
Eyes with harderian gland	Spinal cord (thoracic)
Femur with marrow	*Spleen
Gross lesions	Stomach
*Heart	*Testes/Epididymides
Ileum	Thymus
Jejunum	Thyroid glands/Parathyroids
*Kidneys	Tongue
*Liver	Trachea
Lungs/Bronchi	Urinary bladder
Lymph node (mesenteric)	Uterus
*Ovaries	Vagina

*Weighed at scheduled necropsy. Paired organs will be weighed as a unit.

All tissues and organs collected at necropsy will be examined microscopically for all control and high dose animals. In addition, animals found dead or subjected to a moribund sacrifice will also be processed for microscopic examination. If treatment-related lesions are observed at the high dose, those tissues/organs will be examined microscopically for mid and low dose animals.

- 8.7.8 Statistical Analyses: For each sex, Analysis of Variance tests will be conducted on body weight, food consumption, hematology, clinical chemistry and organ weight data. Organ weight analysis will consider weights relative to brain weight. If a significant F ratio is obtained ($p \leq 0.05$), Dunnett's t test will be used for pair-wise comparisons to the control group. Frequency data such as incidence of mortality, gross necropsy observations

and tissues morphology observations will be compared by Fishers Exact Test or Chi-square analyses as necessary.

Quantitative data will be tabulated and presented in the report. In addition to the written report, summary data tables of parameters and variability will be transmitted to the Sponsor on magnetic media (computer diskette) in "ASCII" form. The transcribed data on disk will no longer be considered GLP compliant.

9.0 RECORDS TO BE MAINTAINED:

All data generated during the conduct study, except those that are generated as direct computer input, shall be recorded directly, promptly, and accurately in ink in bound books with prenumbered pages or on worksheets that shall be bound during or at the conclusion of the nonclinical laboratory study. All appropriate computer and machine output shall be bound during or at the conclusion of the study. All data entries shall be dated on the day of entry and signed or initialed by the person entering the data. Any changes in entries for whatever reason (e.g., to correct an error or transposition) shall be made so as not to obscure the original entry, shall indicate the reason for such change, and shall be dated and signed or identified at the time of data input. In computer driven collection systems, the operator responsible for direct input shall be identified at the time of data input. Any changes in computer entries for whatever reason (e.g., to correct an error or transposition) shall be made in such manner so as not to obscure the original entry, if possible, shall indicate the reason for such change, and shall be dated and the responsible individual shall be identified.

All recorded data shall be reviewed, signed, and dated by a knowledgeable person, other than the person making the entry, to assure adherence to procedures and to verify observations.

Upon completion of the study and submission of the final report, all raw data, documentation, specimens, test article reserves and other materials necessary to reconstruct the study will be stored in the TRL archives maintained by Quality Assurance, unless specified by the Sponsor.

All changes or revisions, and reasons therefore, to this protocol once it is approved shall be documented, signed by the Study Director and Sponsor, dated and maintained with the protocol.

Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-7E
UIC/TRL Study No.: 107

10.0 REGULATORY REQUIREMENTS:

This study will be performed in compliance with the UIC/TRL Quality Assurance Program designed to conform with FDA Good Laboratory Practice Regulations and EPA Good Laboratory Practice Standards. The protocol for this study was approved by the UIC Animal Care Committee.

Will this study be submitted to a regulatory agency? Yes

If so, to which agency(ies)? U.S. Food and Drug Administration

Does the Sponsor request that remaining test articles be returned? Yes

Does the Sponsor request that samples of the test article/carrier mixture(s) be returned? No

Contract No.: DAMD17-92-C-2001
Task Order No.: UIC-7E
UIC/TRL Study No.: 107

11.0 PROTOCOL APPROVAL:

STUDY DIRECTOR:

Barry S. Levine 12/3/92
Barry S. Levine, D.Sc., D.A.B.T. Date

QUALITY ASSURANCE:

Ronald Schoenbeck 12/7/92
Ronald Schoenbeck Date

SPONSOR APPROVAL:

George Schieferstein 12-8-92
George Schieferstein, Ph.D. Date
Contracting Officer's
Representative (COR)

COMMENTS FROM THE COR:

PROTOCOL AMENDMENT

Study No.: 107

Title: Thirteen Week Oral Toxicity Study of WR242511 in Rats

1. Page 1 Section 2.0

Change Sponsor Name: U.S. Army Medical Materiel
Development Activity

Reason: Changed to reflect correct name.

2. Page 1 Section 3.0

Change Testing Facility address to:

University of Illinois at Chicago (UIC)
Department of Pharmacology M/C 868
1940 W. Taylor St.
Chicago, IL 60612-7353

Reason: Changed to reflect street address.

3. Page 1 Section 4.0

Change the study dates as follows:

4.2 Proposed Initiation of Dosing: 10/14/93

4.3 Proposed Necropsy Date: 01/13-14/94

4.4 Proposed Study Completion Date
(Draft Study Report): 04/15/94

Reason: Study dates have been finalized.

4. Page 2 Section 5.0

Change from "TEST ARTICLES" to "TEST ARTICLE"

Reason: WR242511 tartrate is the only test article being tested.

PROTOCOL AMENDMENT

Study No.: 107

Title: Thirteen Week Oral Toxicity Study of WR242511 in Rats

5. Page 2 Section 5.2

A. Change the TRL Chemical No. "0930614" to "1720614"

B. Change the Physical Description to "Yellow powder"

Reason: A different composition of the test article was supplied by the Sponsor [tartrate (yellow powder) instead of diphosphate (orange powder) which was previously tested and assigned number 0930614].

6. Page 2 Section 6.0

A. Change the Toxicologist from "E. Marianna Furedi-Machacek, D.V.M." to "Clyde W. Wheeler, Ph.D."

B. Change the Analytical Chemist from "Ian Tebbett, Ph.D." to "Adam Negrusz, Ph.D."

Reason: Dr. Furedi-Machacek and Dr. Tebbett resigned from UIC.

7. Page 3 Section 7.3

Change the number of animals per sex to "40 Males and 40 Females"

Reason: Mistake in protocol.

8. Page 3 Section 7.9

A. Change humidity range from "(40-70%)" to "(30-70%)"

B. Change cage size to "840 cm²"

C. Change "DHEW (NIH) No. 86.23" to "DHHS (NIH) No. 86.23".

Reason: Humidity range changed to conform with recommended levels in DHHS (NIH) No. 86.23, and cage size was incorrectly described.

PROTOCOL AMENDMENT

Study No.: 107

Title: Thirteen Week Oral Toxicity Study of WR242511 in Rats

9. Page 4 Section 8.1

A. Change the dose levels to read as follows:

"Low" = "0.5" mg base/kg/day

"Mid" = "1.5" mg base/kg/day

"High" = "4.5" mg base/kg/day

B. Change sentence to "Dose levels were selected by the Sponsor based upon the results of a two week oral dose range-finding study in rats (UIC/TRL Study No. 106).

Reason: Dose levels have been selected following consultation with the Sponsor.

10. Page 5 Section 8.2

Remove sentence "The recovery animals will be dosed for 91 days."

Reason: Mistake in protocol; there is no recovery period in this study.

11. Page 5 Section 8.5

Change Test Article Vehicle from "0.5% Na⁺carboxymethylcellulose/0.3% Tween 80" to "1% Methylcellulose/0.2% Tween 80".

Reason: Better suspendability was achieved with this vehicle.

12. Page 5 Section 8.6

A. Change sentence "The dosage formulations for each test article will be prepared weekly, if stability and homogeneity data permit," to "The dosage formulations for the test article will be prepared daily by diluting a stock formulation (made weekly) to the appropriate concentration. Stability and homogeneity data obtained from a previous study (UIC/TRL Study No. 106) indicated that the dosing suspensions are stable for 48 hours at the dosage formulations being tested, and the stock formulation is stable for two weeks. The test article will be prepared by ..."

PROTOCOL AMENDMENT

Study No.: 107

Title: Thirteen Week Oral Toxicity Study of WR242511 in Rats

- B. Change sentence "Samples of dosage formulations (including controls) used in Weeks 1, 7 and 13 will be analyzed for test article concentration prior to use" to "A sample of dosage formulations (including controls) used at the onset of Week 1, 7 and 13 will be analyzed for test article concentration prior to use".

Reason: Clarification of protocol.

13. Page 5 . Section 8.7.1

Remove sentence "During the recovery period, clinical signs will be recorded in the morning."

Reason: Mistake in protocol; there is no recovery period in this study.

14. Page 6 Section 8.7.6

Change sentence to read as follows: "The overnight fasted animals will be anesthetized by inhalation of CO₂/O₂ (≈80:20), ..."

Reason: Clarification of the protocol.

15. Page 7 Section 8.7.7

Add "Diaphragm" to list of tissues/organs list.

Reason: Diaphragm was inadvertently left off the list.

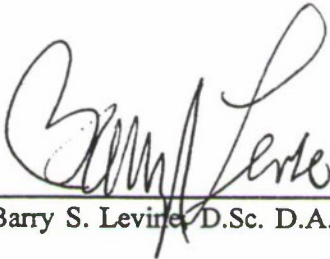
PROTOCOL AMENDMENT

Study No.: 107

Title: Thirteen Week Oral Toxicity Study of WR242511 in Rats

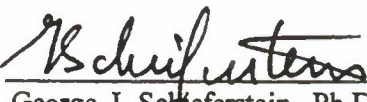
Approvals:

STUDY DIRECTOR:


Barry S. Levine, D.Sc. D.A.B.T.

10/20/93
Date

SPONSOR APPROVAL:


George J. Schieferstein, Ph.D.
Contracting Officer's
Representative (COR)

7/19/94
Date

DRAFT

PROTOCOL AMENDMENT

Study No.: 107

Title: Thirteen Week Oral Toxicity Study of WR242511 in Rats


16. Page 7 Section 8.7.8

Indicate that organ weight analysis will consider weights relative to brain weights only. Analysis will not consider absolute weights or weights relative to body weight as previously indicated.

Reason: Sponsor requested change in the protocol.

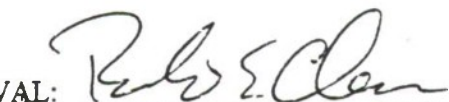
Approvals:

STUDY DIRECTOR:


Barry S. Levine, D.Sc. D.A.B.T.

7/27/94
Date

SPONSOR APPROVAL:


for George J. Schieferstein, Ph.D.
Contracting Officer's
Representative (COR)

10/24/94
Date

DRAFT

APPENDIX 12

Study Deviations

THIRTEEN WEEK ORAL TOXICITY STUDY OF WR242511 IN RATS

Study Deviations*

<u>Deviation Type</u>	<u>Specific Deviation</u>	<u>Effect on Study</u>
Protocol	During the quarantine period, on one occasion, the relative humidity was -2% outside the specified range in the animal room.	None. This occurrence was not considered to have had an impact on the outcome of the study.
Protocol	Dosage formulations tested in Week 1 were analyzed as the salt, not the base. The dosing and stock suspensions were adjusted prior to re-analysis resulting in $\pm 10\%$ of the doses in terms of salt. Therefore, the dosage formulations used in Week 1 (prepared fresh daily by diluting the stock suspension) were $\approx 25 - 30\%$ lower than their target concentrations.	Negligible; all of the other dosing suspensions used in Weeks 2 - 13 were prepared correctly and the other dosage suspensions which were tested were within 10% of their target concentration in terms of the base.
Protocol	Because the thymus could not always be identified at fixed tissue trimming due to its small size, the microscopic examination of thymus sections was not performed for the following high dose animals which were found dead (#366, #367 and #368).	Negligible; thymic lymphocyte depletion was observed as a test article-related change in other high dose males. Thymic involution often occurs in moribund animals in response to stress.

*The detailed "Deviation Reports" are contained in the raw data which are archive at the University of Illinois at Chicago, Department of Pharmacology, Chicago, Illinois.

The above deviations did not affect the integrity of the study.

Barry S. Levine, D.Sc., D.A.B.T.

Date